MAYARA MOLEDO PICANÇO

FORECASTING DISTRIBUTION OF ORAL TRANSMISSION CHAGAS DISEASE VECTORS USING ARTIFICIAL INTELLIGENCE TOOLS

Thesis submitted to the Entomology Graduate Program of the Universidade Federal de Viçosa in partial fulfillment of the requirements for the degree of *Doctor Scientiae*.

Advisor: Raul Narciso Carvalho Guedes

Co-advisor: Ricardo Siqueira da Silva

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ABSTRACT

PICANÇO, Mayara Moledo, D.Sc., Universidade Federal de Viçosa, July, 2024. **Forecasting distribution and oral transmission of Chagas disease vectors using artificial intelligence tools**. Advisor: Raul Narciso Carvalho Guedes. Co-advisor: Ricardo Siqueira da Silva.

Chagas disease is a neglected sickness caused by the protozoan *Trypanosoma cruzi*, which is transmitted by kissing bugs (Hemiptera: Reduviidae: Triatominae). Currently, six to seven million people have this disease and around 75 million people worldwide are at risk of infection. In recent years, oral infection has been the prevalent form of transmission in the Brazilian Amazon, which is associated with the consumption of açaí (*Euterpe oleracea*). Artificial intelligence (AI) tools can be used to determine models with good predictive capacity for complex systems such as those involved in disease transmission. Thus, this thesis aimed to determine models of spatiotemporal dynamics of oral transmission of Chagas disease using AI tools. The thesis was divided into two chapters: (i) modeling key factors influencing the oral transmission of Chagas disease using artificial neural networks, and (ii) predicting current and future distribution dynamics of kissing bugs and palm species associated with oral Chagas disease transmission. Atmospheric pressure, size of the cultivated area, and time elapsed since the beginning of the açaí harvest positively affected the disease's oral transmission rate, while air temperature, rainfall, and wind speed negatively affect transmission. The developed artificial neural network (ANN) model allowed strong predictive capacity for the disease's oral transmission rate across different regions and months over a seven-year period. Ecological niche models determined using MaxEnt indicate high suitability for *Rhodnius* kissing bugs in northern South America, southern Central America, central Africa, and Southeast Asia. An increase in areas with high climatic suitability is expected by 2040 for these kissing bugs. Climate change will likely lead to an increase in the areas of the world suitable for *Rhodnius* kissing bug species involved in the oral transmission of Chagas disease. In the Amazon, where the Chagas disease oral transmission rate is high, measures must be taken for its prevention, especially during the açaí harvest season.

Keywords: Triatominae. Distribution dynamics. Climate change. Epidemiology. Emerging risks.

RESUMO

PICANÇO, Mayara Moledo, D.Sc, Universidade Federal de Viçosa, Julho de 2024. **Previsão da distribuição de vetores de transmissão oral da doença de Chagas usando ferramentas de inteligência artificial**. Orientador: Raul Narciso Carvalho Guedes. Coorientador: Ricardo Siqueira da Silva.

A doença de Chagas é uma doença negligenciada causada pelo protozoário *Trypanosoma cruzi* e transmitida por barbeiros (Hemiptera: Reduviidae: Triatominae). Atualmente, seis a sete milhões de pessoas têm essa doença e cerca de 75 milhões de pessoas no mundo estão em risco de infecção. Nos últimos anos, a infecção oral tem sido a forma prevalente de transmissão da doença na Amazônia brasileira, que está associada ao consumo de produtos do açaí (*Euterpe oleracea*). As medidas mais eficientes na prevenção de doenças que têm insetos como vetores é o controle destes artrópodes. As ferramentas de inteligência artificial (IA) podem ser usadas na determinação de modelos preditivos de sistemas complexos como aqueles envolvidos na transmissão de doenças. Assim, essa tese teve o objetivo de determinar modelos de dinâmica espaço-temporal dos fatores de transmissão oral da doença de Chagas e realizar revisão de literatura sobre os métodos de manejo de barbeiros de Chagas utilizando ferramentas de IA. A tese foi dividida em dois capítulos: (i) modelagem dos principais fatores que influenciam a transmissão oral da doença de Chagas usando redes neurais artificiais, e (ii) dinâmica de distribuição atual e futura de barbeiros e espécies de palmeiras associadas à transmissão oral da doença de Chagas. A pressão atmosférica, o tamanho da área cultivada e o tempo decorrido desde o início da colheita do açaí afetaram positivamente a taxa de transmissão oral da doença, enquanto a temperatura do ar, a precipitação e a velocidade do vento tiveram efeitos negativos. A rede neural artificial (RNA) obtida demonstrou forte capacidade preditiva para a taxa de transmissão oral da doença em diferentes regiões e meses durante um período de sete anos. Os modelos de nicho ecológico determinados usando o programa MaxEnt indicam alta adequação para espécies de barbeiros *Rhodnius* no norte da América do Sul, sul da América Central, África central e sudeste da Ásia. Deverá ocorrer aumento das áreas com alta adequação climática até 2040 para esses barbeiros. As mudanças climáticas deverão ocasionar aumento das áreas do mundo adequadas as espécies de *Rhodnius* envolvidas na transmissão oral da doença de Chagas. Na Amazônia, onde é alta a taxa de transmissão oral da doença de Chagas,

deve-se realizar medidas para evitar esta transmissão sobretudo na época de colheita do açaí.

Palavras-chave: Triatominae. Dinâmica de distribuição. Mudanças climáticas. Epidemiologia. Riscos emergentes

SUMMARY

1. GENERAL INTRODUCTION

Neglected diseases are a group of infectious diseases that mainly affect poor and marginalized populations in tropical and subtropical regions (Hotez et al., 2007; Hotez et al., 2014; Engels & Zhou, 2020). They are regarded as neglected because they are a target of scarce attention in research, treatment development, and funding, especially compared to diseases more prevalent in developed countries (Hotez et al., 2014; Engels & Zhou, 2020). This not only represents a public health problem but also perpetuates the cycle of poverty, as affected populations often do not have access to adequate health services (Engels & Zhou, 2020).

Among the most well-known neglected diseases are Chagas disease, dengue fever, leishmaniasis, schistosomiasis, lymphatic filariasis, onchocerciasis, and rabies (Hotez et al., 2007; Hotez et al., 2014; Engels & Zhou, 2020). These diseases can cause a wide range of symptoms, from chronic debilitating conditions to death (Hotez et al., 2014). Even though they affect more than two billion people, they generally do not attract the same level of interest or resources as other diseases such as HIV/AIDS, tuberculosis, and malaria (Engels & Zhou, 2020). This is partly because it predominantly affects populations with little political or economic influence (Hotez et al., 2007; Hotez et al., 2014; Engels & Zhou, 2020). Consequently, there is a lack of financial incentive for the pharmaceutical industry to invest in research and development of new treatments (Hotez et al., 2007; Hotez et al., 2014; Engels & Zhou, 2020).

Chagas disease, or American Trypanosomiasis, is a severe public health problem that causes major social and economic problems (Hotez et al., 2014). Chagas disease is prevalent in 21 Latin American countries (Pinheiro et al., 2017). In addition, it has caused infections in the United States, Europe, and the Western Pacific region (Bonney, 2014). The protozoan *Trypanosoma cruzi* causes this disease and can be transmitted to humans through different routes (Hotez et al., 2014; Benziger et al., 2017). In addition, several mammals act as natural reservoirs for this protozoan (Abad-Franch et al., 2021). This disease can be transmitted by the bite/feces of kissing bugs (Hemiptera: Reduviidae: Triatominae), consumption of contaminated food, blood transfusion, organ transplantation, congenital transmission, and laboratory accidents (Benziger et al., 2017). Chagas disease can present two clinical phases: the initial or acute phase and the chronic phase (Benziger et al., 2017). The acute phase (4 to 10 days after the bite) is mainly asymptomatic and may progress to the chronic phase in which the individual can suffer cardiac and/or digestive complications (Benziger et al., 2017).

The World Health Organization estimates that about 6 to 7 million people are infected with *T. cruzi* globally, with about 30,000 new cases per year and more than 14,000 deaths per year (WHO, 2022). People currently affected by this disease reside in South American countries (WHO, 2022). In northern Brazil, Chagas disease is considered an emerging disease, and, in recent years (2001-2018), outbreaks of this disease have occurred (Oliveira et al., 2018; Santos et al., 2020).

The current scenario of Chagas disease transmission is different from what occurred in the past. Brazil is the country with the highest number of cases of the disease in the world. In the past, the highest numbers of Chagas disease cases occurred in the Central-West, Southeast, and Southern regions, especially in rural areas (Coura and Dias, 2009). The main vector species of the disease was *Triatoma infestans*, which has domestic habits. In this situation, the key points of control actions were improving homes and facilities and carrying out chemical control of kissing bugs in these places (Dias & Schofield, 2004; Coura & Dias, 2009).

In recent years, outbreaks of the acute form of Chagas disease, especially in the Amazon region, have increased (Shikanai-Yasuda & Carvalho, 2012; Costa et al., 2017; Oliveira et al., 2018; Santos et al., 2020). Epidemiological investigations showed that the majority of these outbreaks are due to the oral transmission of the disease through the consumption of juices and other by-products of the açaí palm tree *Euterpe oleracea* Mart, 1824 (Ricardo-Silva et al., 2012; Shikanai-Yasuda & Carvalho, 2012; Costa et al., 2017; Oliveira et al., 2018; Santos et al., 2020). This transmission involves both the consumption of contaminated food and the vectorial transmission by these insects attracted by the light used in the fruit harvest and post-harvest activities (Shikanai-Yasuda & Carvalho, 2012; Costa et al., 2017; Oliveira et al., 2018; Santos et al., 2020). The kissing bugs *Rhodnius robustus* Larrousse and *Rhodnius pictipes* Stal (Hemiptera: Reduviidae: Triatominae) are the main vector species of Chagas disease associated with oral transmission (Valente et al., 1999; Coura et al., 2002; Ricardo-Silva et al., 2012).

These insects are closely associated with palm trees with large crowns, such as maripa palm (*Attalea maripa* (Aubl.) Mart.) and moriche palm or buriti (*Mauritia* *flexuosa* L.), which construct nests and feed on the blood of animals searching for refuge and nesting in these palms tree (Gaunt & Miles, 2000). Maripa palm is common in the Amazon rainforest and other tropical areas of Brazil, while moriche palm flourishes in moist and swampy areas of the Amazon basin (Smith, 2015). These palm species serve as suitable habitats for triatomines and play a significant role in the epidemiology of Chagas disease in these regions, especially if the distances between palms and dwellings are shorter (Dias et al., 2014; Erazo & Cordovez, 2016; Magalhães et al., 2021).

During açaí harvesting, there is a surge in vector-borne infections attributed to either the production of volatile compounds mimicking the mating pheromones of female kissing bugs or the insect attraction to light sources used in the fruit harvest and post-harvest activities resulting in their fall into açaí containers (Nóbrega et al., 2009; Filigheddu et al., 2017; Guhl, 2017; Ferreira et al., 2018). Although kissing bugs are present in açaí, they do not nest in them due to the relatively small size of their crown and the absence of suitable shelter and nesting sites for other animals that serve as food sources for these vectors (Dias et al., 2014; Magalhães et al., 2021).

Although oral Chagas disease infection is a highly relevant topic, knowledge gaps persist due to limited resources and the complexity of the subject. To this end, modeling the main factors that influence the oral transmission of Chagas disease using artificial neural networks and the current and future distribution dynamics of kissing bugs and associated palm species is essential to understand better the conditions that facilitate the spread of the disease. Artificial neural networks can analyze large volumes of complex data, revealing non-obvious patterns and relationships between environmental and biological variables (Jeyakodi et. al, 2023; Jillahi & Iorliam, 2024). This allows the prediction of outbreaks, the identification of high-risk areas, and the development of effective control strategies. Understanding the spatial and temporal distribution of vectors and hosts helps implement specific preventive measures adaptable to climate and environmental changes, contributing significantly to reducing the incidence and spread of Chagas disease (Freeman, 2015; Santana et. al, 2019).

Thus, this thesis aimed to determine models of spatiotemporal dynamics of the oral transmission factors of Chagas disease using AI tools. This thesis comprises of two chapters: (i) modeling key factors influencing the oral transmission of Chagas disease using artificial neural networks, and (ii) current and future distribution dynamics of kissing bugs and palm species associated with oral Chagas disease transmission.

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CHAPTER 1: Modeling key factors influencing the oral transmission of Chagas disease using artificial neural networks

ABSTRACT

Chagas disease (CD) is a significant, yet neglected disease primarily transmitted by insect vectors. Recently, the consumption of contaminated food, such as açaí (*Euterpe oleracea*), has recently increased levels of oral CD infections. While predicting the incidence rates and identifying the driving factors of this transmission is crucial, no studies have yet developed models for this purpose. This work aimed to develop an artificial neural network (ANN)-based model to predict the oral transmission rate of CD and identify the key factors influencing this transmission. The selected ANN features a logistic activation function, a resilient backpropagation learning algorithm, and three neurons in the hidden layer. Among the 3960 ANNs evaluated, the chosen model's prediction showed the highest correlations with oral transmission rates during both the training and validation stages. Atmospheric pressure, the size of the cultivated area, and the time elapsed since the beginning of the açaí harvest positively affected the disease's oral transmission rate, while air temperature, rainfall, and wind speed had negative effects. The determined ANN demonstrated strong predictive capacity for the oral transmission rate of the disease across different regions and months over a seven-year period. Therefore, the ANN developed in this study is promising for predicting the oral transmission of CD.

Keywords: climate, neglected disease, vector transmission, açaí, machine learning modeling.

1. INTRODUCTION

Chagas disease, caused by the protozoan *Trypanosoma cruzi* Chagas, is one of the most neglected diseases in the world (Pinheiro et al., 2017; Sangenito et al., 2020). It is endemic to Brazil and is primarily transmitted by kissing bugs (Hemiptera: Reduviidae: Triatominae). While several routes of transmission exist, the bite and feces of insect hosts are the most common. In recent years, however, the incidence of oral disease transmission has increased (Guhl, 2017; Ferreira et al., 2018), driven by food contamination and human habits (Guhl, 2017; Ferreira et al., 2018).

Food contamination occurs through exposure to triatomine kissing bugs and their feces during harvesting, preparation, or storage (Nóbrega et al., 2009; Ricardo-Silva et al., 2012; Costa et al., 2017; Ferreira et al., 2018; Oliveira et al., 2018). This mode of transmission has gained relevance lately, particularly in Latin America, likely due to the increased popularity of palm-based products (Nóbrega et al., 2009; Ricardo-Silva et al., 2012; Costa et al., 2017; Ferreira et al., 2018; Oliveira et al., 2018). This form of transmission presents a more severe and rapidly progressive clinical picture compared to the vectorial transmission of the disease (Nóbrega et al., 2009; Ricardo-Silva et al., 2012; Costa et al., 2017; Ferreira et al., 2018; Oliveira et al., 2018). Açaí (*Euterpe oleracea* Mart.), a staple in the Brazilian Amazon, is among the foods associated with the oral transmission of Chagas disease in northern South America (Nóbrega et al., 2009; Costa et al., 2017; Ferreira et al., 2018).

Açaí plantations are crucial for the Amazon region and have economic, alimentary, social, and environmental significance (Reymão et al., 2020; Quaresma and Euler, 2023). Açaí serves as an economic engine, generating jobs and income for small farmers and riverside communities, and boosting the local economy with growing international demand (Reymão et al., 2020; Quaresma and Euler, 2023). Each hectare of açaí plantation in the northern Brazil generates an annual income of US$5349 (IBGE, 2022). Nutritionally, açaí is prized for its rich content of antioxidants, fiber, and vitamins (Reymão et al., 2020; Quaresma and Euler, 2023). It is an important food in the Amazonian diet and has gained global popularity as a "superfood" (Laurindo et al., 2023). Socially, açaí plantations strengthen community and cultural ties, promote social cohesion, and reduce rural exodus (Reymão et al., 2020). Additionally, producer cooperatives improve negotiation conditions and market access (Reymão et al., 2020). Environmentally, sustainable açaí cultivation preserves Amazonian biodiversity, provides wildlife habitat, and contributes to tropical forest conservation, enhancing soil quality and water retention (Reymão et al., 2020; Quaresma and Euler, 2023).

Among the species of kissing bugs associated with the oral transmission of Chagas disease, those of the genus *Rhodnius* (Hemiptera: Reduviidae: Triatominae) are generally the most significant (Valente et al., 1999; Coura et al., 2002; Ricardo-Silva et al., 2012). Other genera within the Triatominae subfamily may also be involved, as all species in this subfamily are potential vectors of *T. cruzi* (Galvão, 2021). *Rhodnius* species implicated in the oral transmission of Chagas disease inhabit palm trees with large crowns, such as maripa palm (*Attalea maripa* (Aubl.) Mart.) and moriche palm (*Mauritia flexuosa* L.f.), and only sporadically visit human habitations when artificial lights disturb their flights (Aguilar et al., 2007; Bérenger et al., 2009; Castro et al., 2010; Marchant et al., 2016; Marchant et al., 2021; Fabian at al., 2024). Both palm tree species are frequent in the Amazon basin, and the kissing bugs tend to move to açai palms during the harvest season (Aguilar et al., 2007; Bérenger et al., 2009; Castro et al., 2010; Marchant et al., 2016; Marchant et al., 2021; Fabian at al., 2024).

Climatic factors also influence the incidence of insect-borne diseases (Souza and Weaver, 2024). These factors affect kissing bugs, human behavior, and the phenological stages of plants associated with oral transmission of the Chagas disease (Di Iorio and Gürtler, 2017; Moraes et al., 2020; Souza and Weaver, 2024). Among the climatic elements, air temperature and rainfall are generally the most critical for disease transmission rates (Cordovez et al., 2014). Additionally, winds can affect the dispersal of insect vectors (Schmidt et al., 2022), while atmospheric pressure influences rainfall and wind incidence (Lutgens et al., 2019), which in turn affect insect populations.

Space-time dynamics models are statistical tools used to estimate the behavior of variables in a region over time. They predict phenomena and identify their regulating factors (Wang et al., 2022). The epidemiological data related to disease transmission rates are complex and vary significantly over time and location (Kanankege et al., 2020). Conventional statistical models are generally inadequate to predict the behavior of complex variables (Oberpriller et al., 2021), such as disease transmission rates over extended periods and large areas (Kanankege et al., 2020). In contrast, machine learning models are artificial intelligence tools well-suited for predicting complex data (Hu et al., 2022).

Among the machine learning models are artificial neural networks (ANN), which simulate the functioning of neurons in the human nervous system, where the data processing units act as artificial neurons. These networks consist of three layers: (i) input, (ii) hidden, and (iii) output. The model's predictors are in the input layer, while data processing occurs in the hidden layer through activation functions and learning algorithms. The activation function determines whether each neuron will be activated, and the learning algorithms perform network calculations. The variable to be predicted is in the output layer. Determining an ANN involves two steps: training, where the model is developed and selected, and validation, where the selected model is tested and validated (Du and Swamy, 2019; Farias et al., 2022).

Some deep learning and ANN models can identify *T. cruzi* vectors (Khalighifar et al., 2019; Rabinovich et al. 2021; Miranda et al., 2024). However, despite the importance of oral transmission of Chagas disease, no studies to date have developed models using ANNs to predict its incidence rate and identify the influencing factors. Therefore, this study aimed to develop an ANN model to predict the oral transmission rate of Chagas disease and identify the factors involved in this process.

2. MATERIAL AND METHODS

2.1. Data collection

Data were collected on the oral transmission rate of Chagas disease, açaí palm plantations, maripa and moriche palm trees, kissing bugs of the *Rhodnius* genus, and climatic elements. These data were used because they are involved in the oral transmission of Chagas disease (Guhl, 2017; Ferreira, et al., 2018). For Chagas disease, data from all of Brazil were utilized, while for the other variables, data from the state of Pará, Brazil, was used. This choice was made because the state of Pará has the highest incidence rates of oral transmission of Chagas disease (Figure 1).

The oral transmission rates of Chagas disease were obtained from the SINAN database from 2016 to 2022 (MS, 2024). Confirmed cases of the disease were selected, and the mode of infection of the disease was identified. For açaí plantations, data on the area under cultivation and the fruit harvest period were used. The areas with açaí plantations were obtained from the Brazilian Institute of Geography and Statistics (IBGE) (Reymão, et al., 2020). The harvest times for açaí fruits were obtained from Oliveira and Tavares (2016).

Variables from the fruit harvest time and records of their occurrences were used to assess the maripa and moriche palm trees. Data from occurrence records were used to study *Rhodnius* kissing bugs. Data on the occurrence of kissing bugs and these palm trees were obtained from scientific publications, reports, and databases contained in the Global Biodiversity Information Facility (GBIF http://www.gbif.org/), Web of Science, Science Direct, Google and PubMed, and MEDLINE (Silva et al., 2018; Ramos et al., 2019). Google Earth Pro (version 7.3) (https://earth.google.com) was used to determine the latitude and longitude of the locations of these kissing bugs and palm trees.

Daily average data on relative air humidity, wind speed, atmospheric pressure, photosynthetically active radiation, clarity index, dew point, thermal range, and air temperatures (maximum, average, and minimum) were obtained from NASA Prediction of Worldwide Energy Resources (NASA, 2024). These data were collected for the central part of the microregions of Belém (1.4277°S, 48.1725°W, altitude 21m), Cametá (2.48601°S, 49.6569°W, altitude 20m), and Furos de Breves (1.1063°S, 50.7170°W, altitude 16m). This was done because these microregions have the highest incidence of oral transmission of Chagas disease (Figure 2A).

2.2. Artificial neural network model data preprocessing

Daily data on climatic elements from the Belém, Cametá, and Furos de Breves microregions from January 2016 to December 2022 were subjected to Pearson correlation analysis. Variables with a correlation modulus greater than 0.50 with the greatest biological significance for the phenomenon studied were selected. This was done to reduce the number of predictors in the ANN models (Wu et al., 2010; Alver et al., 2020).

Time lags of 0, 7, 15, 30, 60, 90, 120, 150, and 180 days were calculated for the selected climatic elements. Each time lag represents the average of climate data over a specific period before the recorded data of oral Chagas disease infection (0 = day of assessment to 180 = day of assessment plus the previous 179 days). This was done to determine the period during which the climatic elements most affected the studied phenomenon (Farias et al., 2022; Asadgol et al., 2019). The daily, weekly, biweekly, and monthly rates of people orally infected with Chagas disease were calculated for each microregion to determine the most suitable response variable for studying oral Chagas disease infection.

The data for each time lag of the climatic elements and oral transmission rate of the disease were randomly divided into two groups using the "sample.split" function of the "caTools" package (Li et al., 2023; Valliant et al., 2024). The first group, containing 70% of the data, was used to train the models. The second group, containing 30% of the data, was used to validate the model selected in the training stage (Cerrejón et al., 2020; Amador et al., 2021).

The input data was centered (subtracting the mean) and scaled using the "scale" function from the "stats" package. This was done to prevent variables with higher values from having greater weight in the model and to speed up model convergence. The response variable was also rescaled to a range of 0 to 1 (Beck, 2018).

2.3. Data analysis

Data analysis was conducted using R 4.1 software (R Core Team, 2022). The number of people infected with Chagas disease was calculated depending on the form of transmission, regions of Brazil, and the states in the country's northern region. Maps were created to show the geographic distribution of oral transmission of Chagas disease, açai plantations, records of the occurrence of *Rhodnius* spp., and the maripa and moriche palm trees in the microregions of the state of Pará.

Variables related to açaí plantations and climatic elements were used as model predictors. This was done because *Rhodnius* kissing bugs and maripa and moriche palm trees are present in all three microregions studied (Figure 2). Therefore, these variables did not affect the variation in the oral transmission rate of Chagas disease. Furthermore, the fruit harvests of maripa and moriche palm trees (Figure 4A) occur at times different from those with higher oral disease transmission rates and did not positively affect this transmission rate.

The mlp function from the RSNNS package was used to determine the artificial neural networks. Four activation functions (identity, logistic, hyperbolic, tangent, and exponential) were used. The models tested 1 to 11 neurons in the hidden layer and up to 100 interactions. The initial weight of each artificial neural network was established randomly, with other arguments for artificial neural networks standardized (Lewis, 2017; Kulkarni et al., 2021; Farias et al., 2022).

A total of 3960 network models were determined. For each artificial neural network, Pearson correlations were calculated between their predictions and data on oral transmission rates of Chagas disease used in the models' training (rt) and validation (rv) stages. The mean absolute error (MAE) associated with each artificial neural network was also calculated. The criteria for selecting the optimal artificial neural network included the highest rt and rv values, the lowest EAM value, the fewest neurons in the hidden layer, and the time lag of climatic element data with biological significance for the studied phenomenon. These criteria ensured the selection of a robust, simple model with accurate predictions, minimal underfitting and overfitting errors, and biological relevance (Kulkarni, et al., 2021; Farias et al., 2022).

The significance of the selected neural network predictors was tested using Olden's algorithm. This analysis was done using the olden function from the NeuralNetTools package. The selected neural network was executed 250 times using a different initial weight each time. These estimates were used to determine the confidence interval for the effect of each predictor at 95% probability (CI95). A predictor was considered significant when its CI95 did not cross the origin (Farias et al., 2022; Holcomb et al., 2023). Curves of variation in the Chagas disease oral transmission rate were determined for each significant predictor using the “partial” function from the pdp package (Zhang et al., 2018; Pizarroso et al., 2020). Finally, variation curves were created for the predicted and observed oral transmission rates of Chagas disease over the years in each studied microregion to evaluate the predictive capacity of this model over time and across different regions (Shanmugam et al., 2022).

3. RESULTS

Oral infection was the predominant form of Chagas disease transmission, accounting for 90.44% of cases, followed by vector transmission at 8.55% and vertical transmission at 0.46% (Figure 1A). The northern region of Brazil had the highest rate of oral transmission of Chagas disease at 95.74%, followed by the northeast region at 3.84% (Figure 1B). Within the northern region, the state of Pará exhibited the highest incidence of oral infection at 83.32%, followed by Amapá at 7.72% and Amazonas at 5.95% (Figure 1C). In Pará, the microregions with the highest incidence of oral transmission were Cametá (15.52%), Furos de Breves (12.42%) and Belém (8.33%) (Figure 2A). Figure 2 illustrates the geographic distributions in Pará of *Rhodnius* kissing bugs, maripa and moriche palm trees, and açaí plantations, all of which are factors involved in the oral transmission of Chagas disease.

The artificial neural network (ANN) with the highest correlation between its predictions and observed data used the monthly oral transmission rate of Chagas disease as the response variable and climate data from the previous 120 days. This ANN showed a significant correlation during both the training stage ($r_t = 0.621$, $t = 10.45$, $df = 174$, $p < 0.0001$) and the validation stage ($r_v = 0.733$, $t = 9.27$, $df = 74$, $p < 0.0001$). It had one of the lowest mean absolute errors (MAE = 0.180) and employed three neurons in the hidden layer. The logistic activation function and the resilient backpropagation learning algorithm were used (Table 2), making this ANN the selected model for predicting the oral transmission rate of Chagas disease.

The diagram of the optimal ANN is shown in Figure 3. It consists of three layers of neurons: an input layer with six neurons representing initial predictors - area with açaí plantations in hectares (I1), time after the start of the açaí harvest in days (I2), and the average data on climate variables over the last 120 days (I3 to i6); a hidden layer with three neurons (H1, H2, and H3); and an output layer with a neuron for the monthly oral infection rate of Chagas disease (O1). The climatic variables included average air temperature in °C (I3), rainfall in mm/day (I4), wind speed in m/s (I5), and atmospheric pressure in kPa (I6).

The harvest seasons extends from August to the end of November for açaí, January to the end of March for maripa palm, and March to the end of August for moriche palm (Figure 4A). Figures 4B, 4C, and 4D show the variations in climatic elements from 2016 to 2022 during the seven years in the Belém (B), Cametá (C), and Furos de Breves (D), microregions of Pará, Brazil. The Belém microregion had an average air temperature of 27.11 °C, average atmospheric pressure of 100.97 kPa, rainfall of 7.78 mm/day, and average wind speed of 0.76 m/s (Figure 4B). The Cametá microregion had an average air temperature of 27.22 °C, average atmospheric pressure of 100.95 kPa, rainfall of 7.49 mm/day, and average wind speed of 0.58 m/s (Figure 4C). The Furos de Breves microregion had an average air temperature of 27.03 °C, average atmospheric pressure of 100.86kPa, rainfall of 6.72 mm/day, and average wind speed of 0.07 m/s (Figure 4D).

The 95% confidence intervals for the effects of the six initial predictors of the selected ANN model did not pass through the origin (Figure 5A). Therefore, the area with açaí plantations, time after the start of the açaí harvest, average air temperature, rainfall, average wind speed, and atmospheric pressure significantly affected the model's monthly rate of Chagas disease oral infection.

Positive correlations were observed between the monthly rate of oral infection of Chagas disease and the size of açaí plantation areas, the time taken to harvest, and atmospheric air pressure. Conversely, negative correlations were observed between the oral transmission rate and average air temperature, rainfall, and wind speed (Figure 5B).

The oral infection rate varied depending on the regions, years, and months. The highest rate was observed in the Cametá microregion, followed by the Furos de Breves and Belém microregion. The rate of oral infection peaked from August to November, with the highest incidence in August and September. The second (2017) and fifth (2020) years of the study showed lower infection rates compared to other years. The oral infection rates predicted by the ANN model closely matched the observed rates over the seven years across the three studied microregions (Figure 6).

4. DISCUSSION

Chagas disease can be transmitted to humans through various routes including the bite or feces of kissing bugs (Hemiptera: Reduviidae: Triatominae), consumption of contaminated food, blood transfusion, organ transplantation, congenital transmission, and laboratory accidents (Benziger et al., 2017; Lidani et al., 2017). Historically, vector transmission through contact with infected triatomine feces was the most prevalent form (Pinheiro et al., 2017). However, improvements in housing and effective kissing bug control programs have reduced vector transmission (Westphalen et al., 2012). Currently, oral transmission is the main form of Chagas disease transmission, accounting for 90.44% of cases, with the highest incidence in Brazil's northern region (95.74% of oral transmission), particularly in the state of Pará (83.32% of oral transmission). Understanding the factors influencing the rate and distribution of oral transmission is crucial for implementing effective control measures.

The artificial neural network (ANN) model developed in this study proved robust and accurate in predicting the oral transmission rate of Chagas disease. Its robustness is evidenced by the highest correlation between its predictions and actual transmission rates among the 3960 models evaluated during both the training and validation stages. This high predictive power is attributed to the logistic activation function and resilient backpropagation learning algorithm used in the model (Kiliçarslan and Celik, 2021; Dodo et al., 2024). The logistic activation function provides the necessary nonlinearity to model complex patterns (Kiliçarslan and Celik, 2021), while the resilient backpropagation learning algorithm ensures efficient and robust training, resulting in accurate and generalizable models (Kiliçarslan and Celik, 2021; Dodo et al., 2024).

The model's accuracy is linked to its low average error and the small number of neurons in the hidden layer. Errors in models can stem from underfitting or overfitting (Bashir et al., 2020). Underfitting occur when the model fails to capture the data's complexity, resulting in low predictive power during training (Pothuganti, 2018). The selected ANN had a low underfitting error, as it showed the highest correlation between predictions and observed oral transmission rates during training among the 3960 models. Overfitting errors arise when a model is too closely tailored to the training data, reducing its predictive power in other contexts (Bejani and Ghatee, 2021). The selected ANN also exhibited low overfitting error, demonstrated by a high correlation between predictions and observed data during validation. A contributing factor to this low overfitting error is the minimal number of neurons in the hidden layer (three neurons), as models with more neurons tend to overfit (Uzair and Jamil, 2020; Bejani and Ghatee, 2021).

The simplicity of the ANN model, which features only six predictors and three neurons in the hidden layer, enhances its interpretability and biological relevance (Elangasinghe et al., 2014; Stangierski et al., 2019). The model's predictors include characteristics of açaí plantations and climatic variables, factors previously linked to the oral transmission of Chagas disease (Barbosa et al., 2016; Santana et al., 2019). Notably, this study is the first to use açaí plantation characteristics to predict the oral transmission rate of Chagas disease. Climatic variables affecting kissing bug populations, were also significant predictors (Parra-Henao et al., 2016, Ravazi et al., 2023). The 120-day time lag for climatic data corresponds to the life cycle duration of kissing bugs associated with oral transmission (Guarneri and Lorenzo,2021; Olaia et al., 2021), reflecting the period during which these insects are exposed to climatic conditions. The model's performance was enhanced by using monthly transmission rate as the response variable, which improved accuracy due to the extended data collection period (Cabanillas and Terzi, 2012).

Both açaí plantations and climatic elements influenced the oral transmission rate of Chagas disease. The impact of açaí plantations is linked to the consumption of *T. cruzi*-contaminated food and activities related to harvesting these fruits (Nóbrega et al., 2009; Ricardo-Silva et al., 2012; Costa et al., 2017; Guhl, 2017; Ferreira et al., 2018; Oliveira et al., 2018, Santos et al., 2020, Filigheddu et al., 2017). The increase in transmission during the açaí harvest is attributed to greater exposure of workers to kissing bugs and contaminated açaí juices (Costa et al., 2017; Ferreira, et al., 2018; Santos et al., 2018). Açaí fruits attract animals, providing blood sources for kissing bugs (Dias et al., 2014; Magalhães et al., 2021), and the volatiles emitted by açaí fruits mimic the sexual pheromones of some kissing bug species, attracting them (Filigheddu et al., 2017; Guhl,2017). Artificial light used during harvesting disrupts the nocturnal flights of kissing bugs, causing them to fall into containers with fruits, leading to contamination (Filigheddu et al., 2017; Guhl,2017).

Regions with larger açaí plantation areas showed higher oral transmission rates due to increased exposure to this mode of transmission (Ricardo-Silva et al., 2012; Shikanai-Yasuda and Carvalho, 2012; Costa et al., 2017). The expansion of areas with açaí plantations has been a trend in recent years (Portilho et al., 2020; Alvez-Valles et al., 2022) and is driven by rising consumption of these fruits (Santana and Costa, 2008; Portilho et al., 2020), bringing significant economic, social, and environmental benefits (Marinho, 2009; Santos et al., 2021). However, this trend has public health implications, requiring measures to reduce oral transmission of Chagas disease. These include health surveillance, public education, strengthening public health services, and research (Shikanai-Yasuda and Carvalho, 2012; Peterson et al., 2005).

Climatic elements such as air temperature, rainfall, wind speed, and atmospheric pressure also affected the oral transmission rate of Chagas disease. High temperatures, rainfall, and wind speeds had negative impacts, while higher atmospheric pressure had a positive correlation with transmission. High temperatures can cause dehydration in kissing bugs and reduce their flight activity (Rocha et al., 2001; Brito et al., 2019). Rainfall negatively impacts transmission due to the mechanical effect of raindrops causing insect mortality and disrupting flight (Day, 2006; Pereira et al., 2018; Bacci et al., 2019). Furthermore, extreme temperatures and rainfall limit human activity, reducing transmission risks (Nawshin et al., 2020; Wanderley et al., 2021). Higher atmospheric pressure, associated with lower rain and wind probabilities, favors kissing bug activity (Lutgens et al., 2019; Azevedo et al., 2023).

This study's findings can guide measures to prevent the oral transmission of Chagas disease. These measures include proper hygiene in the production chain, health surveillance, consuming food from certified sources, and training individuals involved in the açaí harvest and sale (Noya et al., 2015; Oliveira et al., 2019). These actions should be intensified between August and November, the peak period for açaí fruit harvest and oral transmission rates.

In conclusion, the ANN model developed in this study is effective for predicting the oral transmission rate of Chagas disease. It accurately predicts transmission rates across different regions and periods, with key influencing factors including the size of açaí plantation areas, time after the start of the açaí harvest, air temperature, rainfall, wind speed, and atmospheric pressure.

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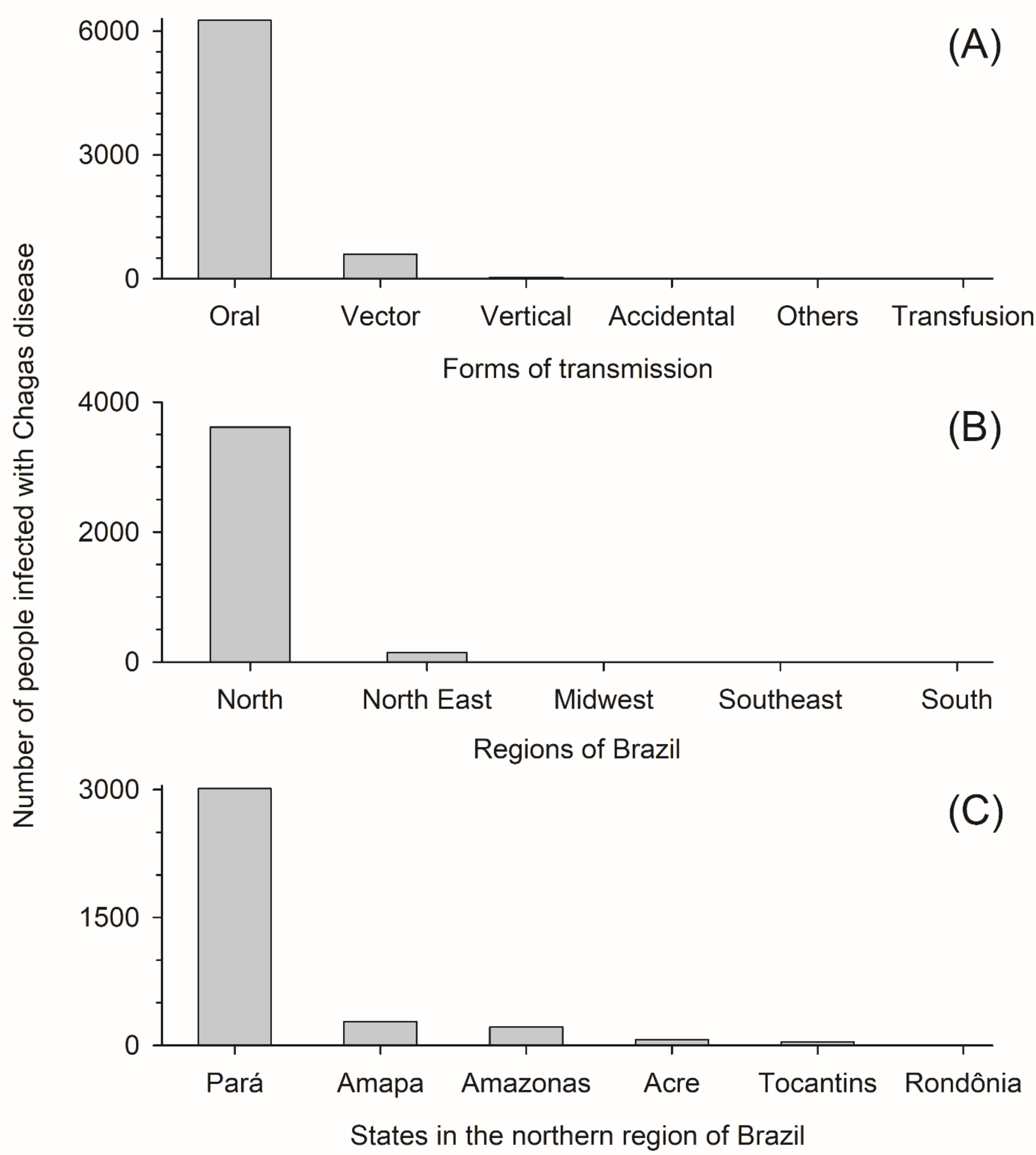

Figure 1. Number of infected people in Brazil with Chagas disease from 2007 to 2022. (A) transmission mode of the disease. (B) Oral transmission of the disease in different regions, (B) states within the northern region of Brazil

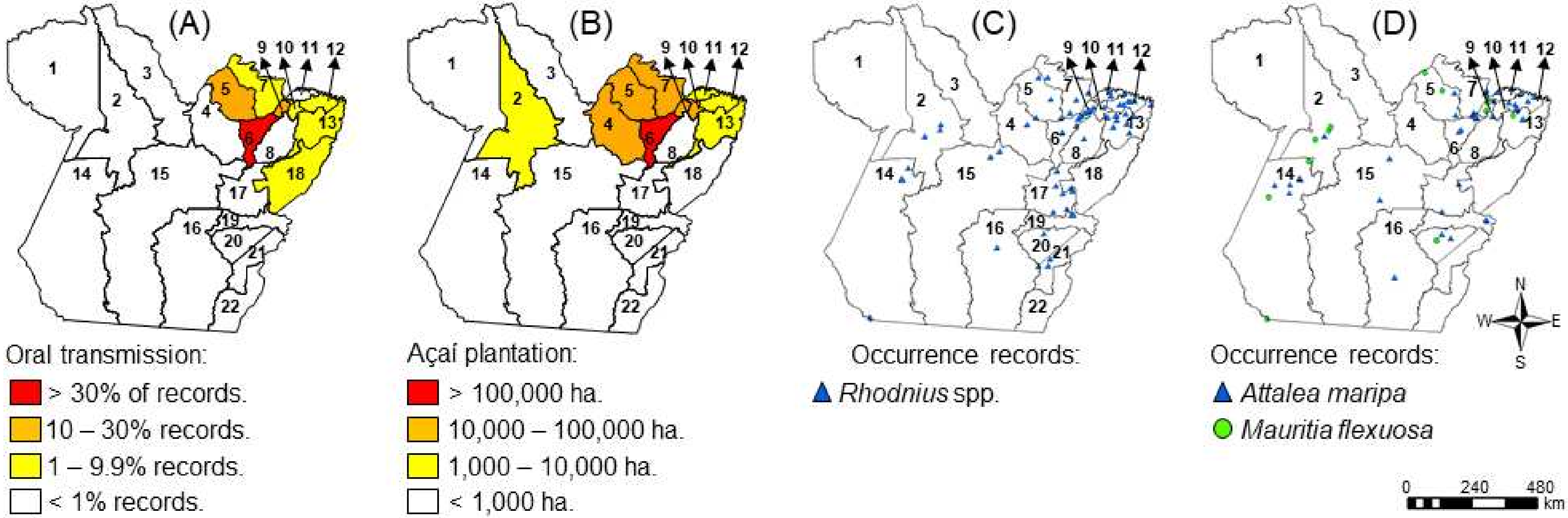

Figure 2. Geographic distribution of (A) oral transmission of Chagas disease, (B) açai plantations, (C) records of occurrence of *Rhodnius* kissing bugs, and (D) records of occurrence of maripa and moriche palm trees in microregions of Pará, Brazil. Microregions: 1 = Óbidos, 2 = Santarém, 3 = Almeirim, 4 = Portel, 5 = Furos de Breves, 6 = Cametá, 7 = Arari, 8 = Tomé-Açu, 9 = Belém, 10 = Castanhal, 11 = Salgado, 12 = Bragantina, 13 = Guamá, 14 = Itaituba, 15 = Altamira, 16 = São Félix do Xingu, 17 = Tucuruí, 18 = Paragominas, 19 = Marabá, 20 = Parauapebas, 21 = Redenção and 22 = Conceição do Araguaia.

Table 1. Pearson correlations between daily data on climatic elements in the microregions of Belém, Cametá, and Furos de Breves from July 2005 to December 2022.

	Air temperature (minimum)	Air temperature (maximum)	Thermal range	Dew point	Clearness index	Photosynthetically active radiation	Atmospheric pressure	Wind speed	Relative humidity	Rainfall
Relative humidity										0.468
Wind speed									-0.070	-0.016
Atmospheric pressure								0.268	0.362	0.068
Photosynthetically active radiation							0.035	0.104	-0.410	-0.504
Clearness index						0.953	0.180	0.085	-0.323	-0.515
Dew point					-0.203	-0.286	0.330	0.071	0.921	0.381
Thermal range				-0.846	0.385	0.468	-0.388	-0.180	-0.908	-0.493
Air temperature (maximum)			0.960	-0.834	0.364	0.457	-0.403	-0.015	-0.963	-0.478
Air temperature (minimum)		0.426	0.155	-0.208	0.042	0.102	-0.167	0.527	-0.466	-0.094
Air temperature (average)	0.611	0.968	0.868	-0.775	0.355	0.441	-0.378	0.114	-0.955	-0.456

Table 2. Topology (NN = number of neurons in the hidden layer, AF = activation function and LA = learning algorithm) and performance metrics (rt and rv = Pearson correlations between predictions and observed data in the training and validation stages and MAE = Mean Absolute Error) of the artificial neural networks (ANNs) with the best performance in each time lag interval (Lag) in days for climatic elements data and daily, weekly, biweekly and monthly oral infection rate of Chagas disease from 2016 to 2022.

Lag	NN	AF§	LA§	rt	rv	MAE	NN	AF§	LA§	rt	rv	MAE
	Daily rate						Weekly rate					
0	9	Sig	Rpr	0.223	0.186	0.045	-	-	-	-	-	-
7	8	Log	Rpr	0.224	0.186	0.045	5	Sig	Rpr	0.435	0.446	0.118
15	6	Sig	Sbc	0.222	0.195	0.047	5	Sig	Rpr	0.442	0.483	0.116
30	8	Log	Rpr	0.238	0.200	0.045	8	Log	Sbc	0.382	0.424	0.118
60	5	Log	Rpr	0.233	0.213	0.045	7	Log	Rpr	0.433	0.459	0.113
90	7	Sig	Rpr	0.239	0.205	0.045	8	Sig	Rpr	0.472	0.503	0.113
120	8	Sig	Rpr	0.246	0.219	0.045	2	Thp	Rpr	0.403	0.461	0.115
150	7	Log	Rpr	0.253	0.236	0.044	10	Sig	Rpr	0.486	0.477	0.111
180	5	Sig	Rpr	0.243	0.230	0.045	4	Log	Rpr	0.427	0.478	0.113
	Biweekly rate						Monthly rate					
15	1	Sig	Scg	0.354	0.465	0.170	-	-	-	-	-	-
30	9	Thp	Rpr	0.563	0.594	0.162	7	Idt	Scg	0.395	0.572	0.171
60	2	Sig	Rpr	0.501	0.532	0.166	3	Log	Rpr	0.598	0.569	0.100
90	3	Sig	Rpr	0.548	0.566	0.162	5	Idt	Sbc	0.485	0.600	0.187
120	2	Sig	Scg	0.431	0.557	0.164	*3	Log	Rpr	0.621	0.733	0.180
150	2	Idt	Sbc	0.424	0.564	0.223	2	Log	Rpr	0.597	0.730	0.168
180	5	Thp	Rpr	0.577	0.566	0.162	10	Log	Scg	0.518	0.729	0.171

* Selected artificial neural network.

§ Idt = identity, Log = logistic, Rpr = resilient backpropagation, Sbc = standard backpropagation, Scg = staggered conjugate gradient, Sig = sigmoid and Thp = hyperbolic tangent.

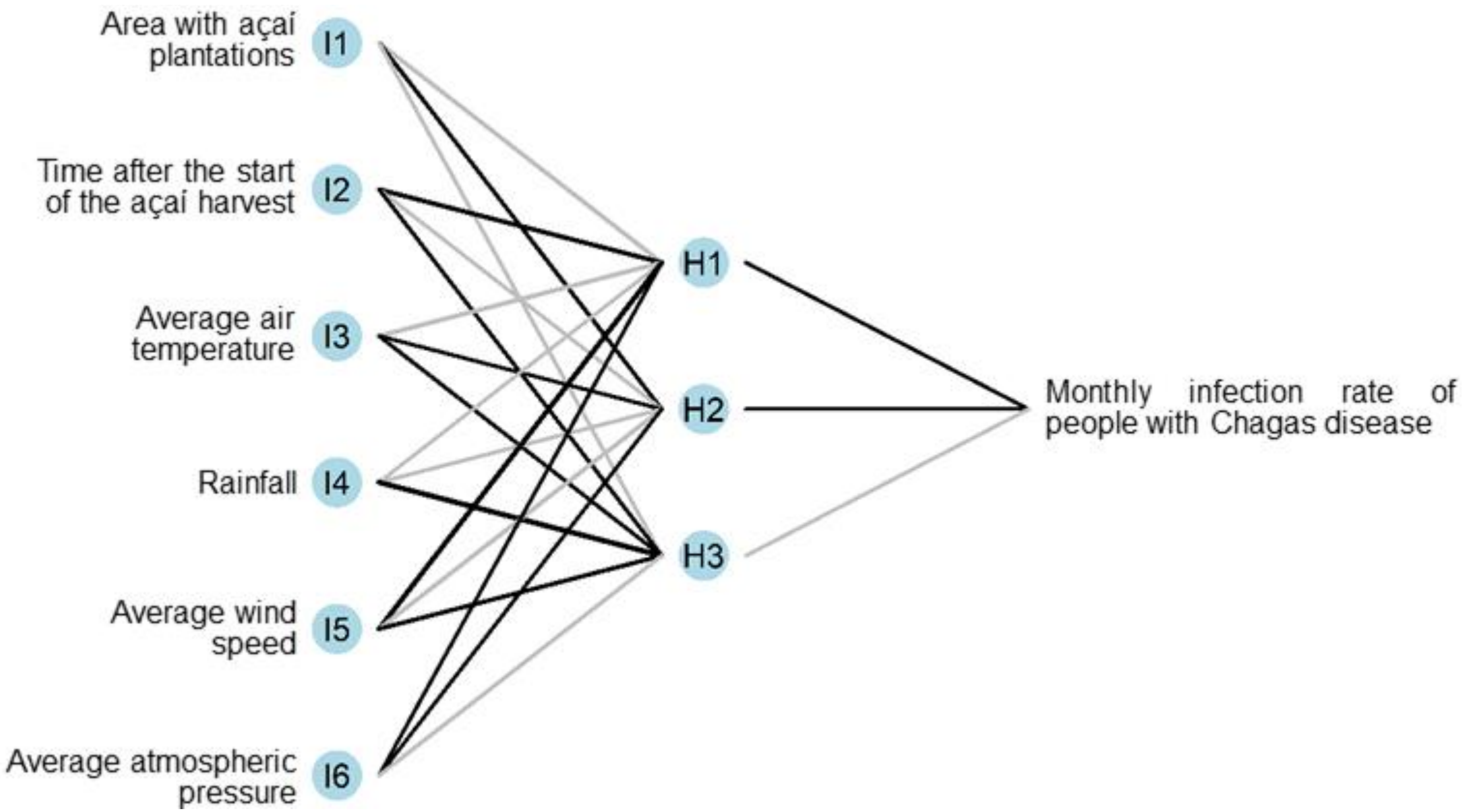

Figure 3. Diagram of the optimal artificial neural network (ANN). This ANN has an input layer with six neurons (I1 to I6), a hidden layer with three neurons (H1 to H3), and an output layer with a single neuron (O1). I1 = Area cultivated with açaí (ha), I2 = time after the start of açaí harvest (days), and I3 to I6 = average data on climate variables over the last 30 days: I3 = average air temperature (°C), I4 = precipitation rainfall (mm/day), I5 = average wind speed (m/s) and I4 = atmospheric pressure (kPa). The black and gray lines represent positive and negative weights between layers, respectively. The thickness of the line corresponds to the relative magnitude of each weight.

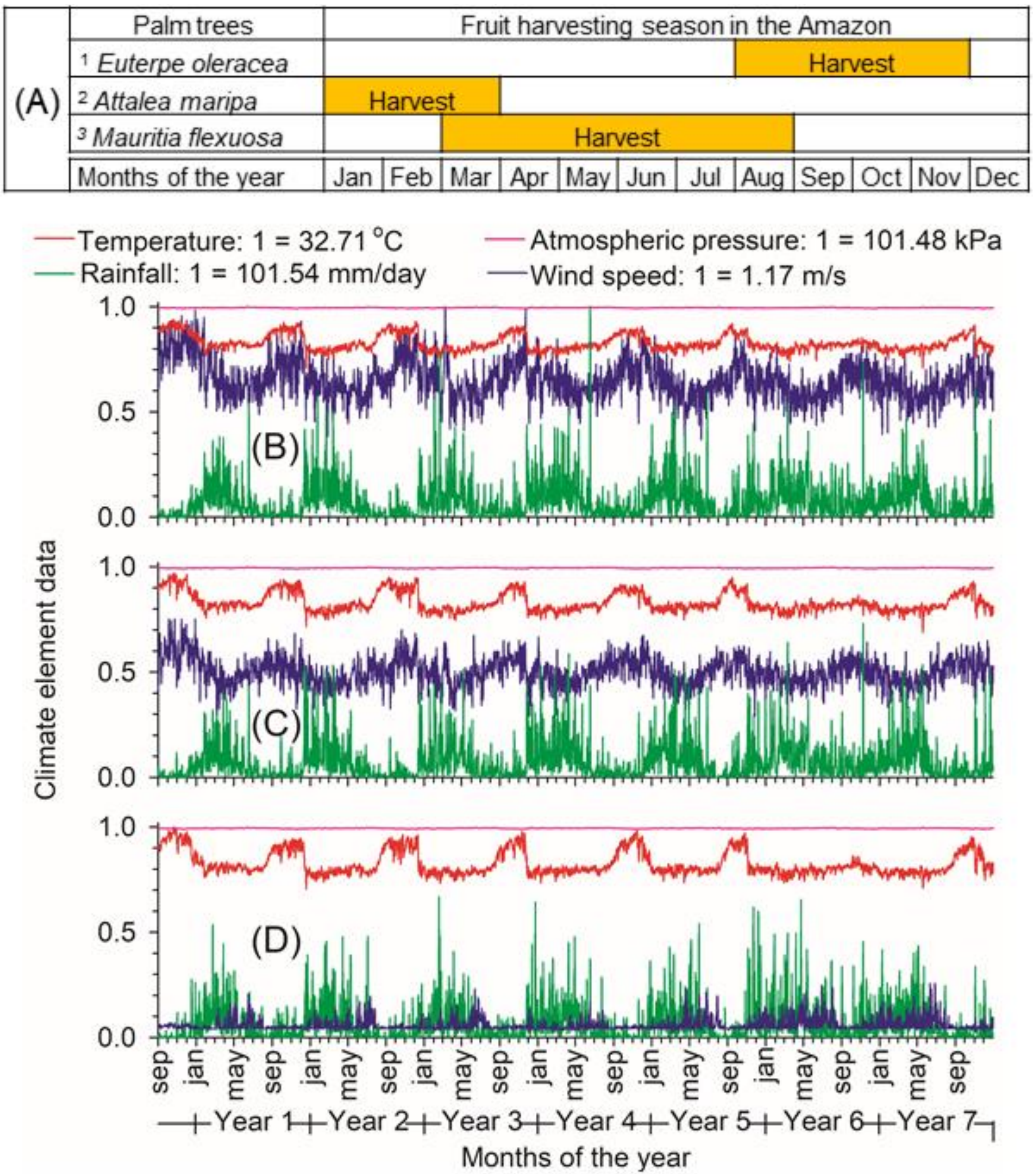

Figure 4. (A) Fruit harvest times of palm trees associated with oral transmission of Chagas disease: maripa palm (Attalea maripa) and moriche palm (Mauritia flexuosa). Sources: 1 Oliveira and Tavares (2016), 2 Bezerra (2011), and 3 Sampaio and Carrazza (2012). (B) Average climatic elements in Belém microregion: average air temperature (°C), atmospheric pressure (kPa), rainfall (mm/day), and wind speed (m/s). (C) Average climatic elements in Cametá microregion: average air temperature (°C), atmospheric pressure (kPa), rainfall (mm/day), and wind speed (m/s). (D) Average climatic elements in Furos de Breves microregion: average air temperature (°C), atmospheric pressure (kPa), rainfall (mm/day), and wind speed (m/s).

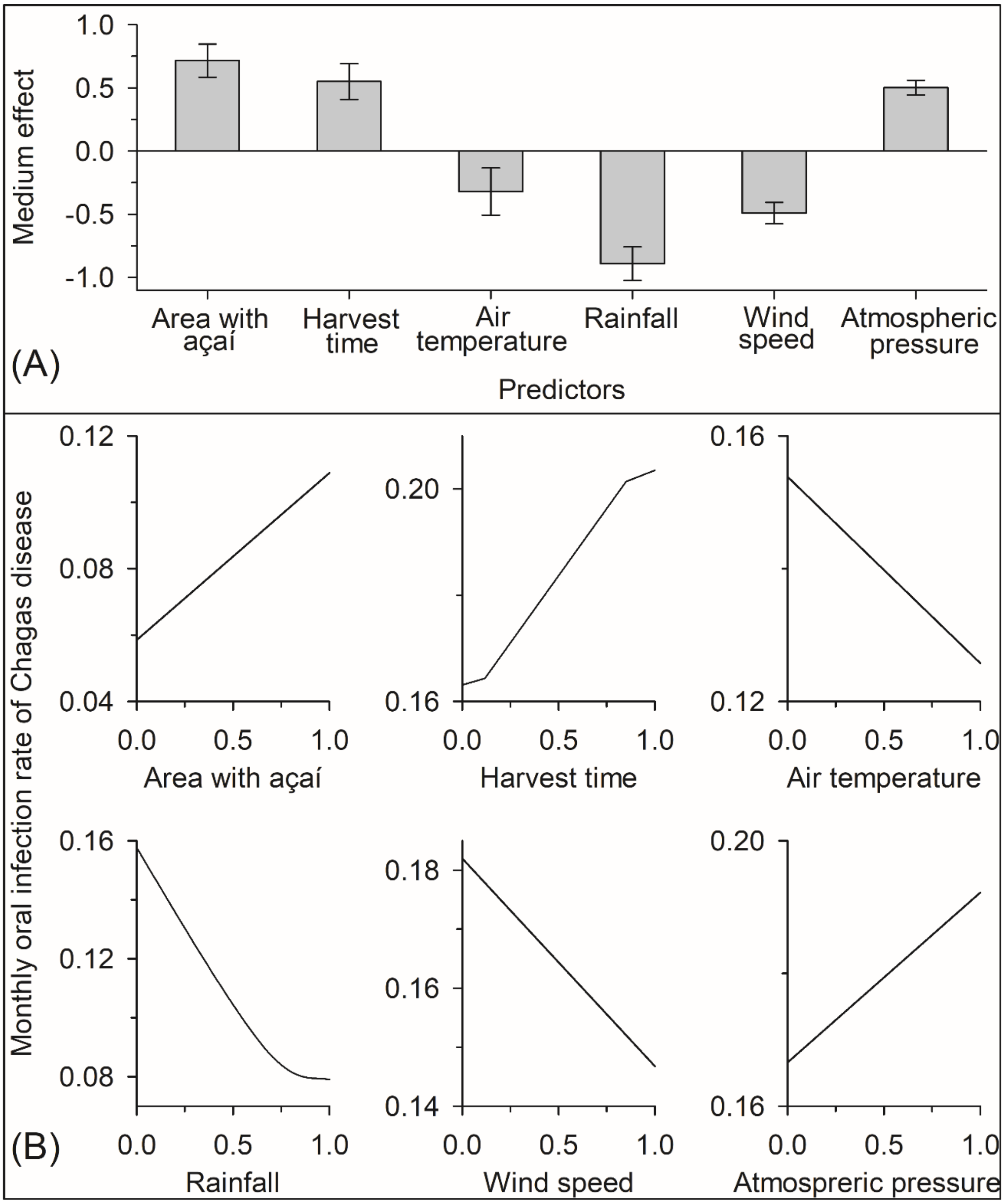

Figure 5. (A) Mean ± 95% confidence interval of the probability of the average effects of the predictors on the monthly oral infection rate of Chagas disease. Predictors include: area with açaí crops (ha), time after the beginning of the açaí harvest (days), average air temperature (°C), rainfall (mm/day), average wind speed (m/s), and average atmospheric pressure (kPa). (B) Variation in the monthly oral infection rate of Chagas disease (1 = 36 people infected per month) as a function of the predictors: area with açaí crops, time after the beginning of the açaí harvest, average air temperature, rainfall, average wind speed, and average atmospheric pressure.

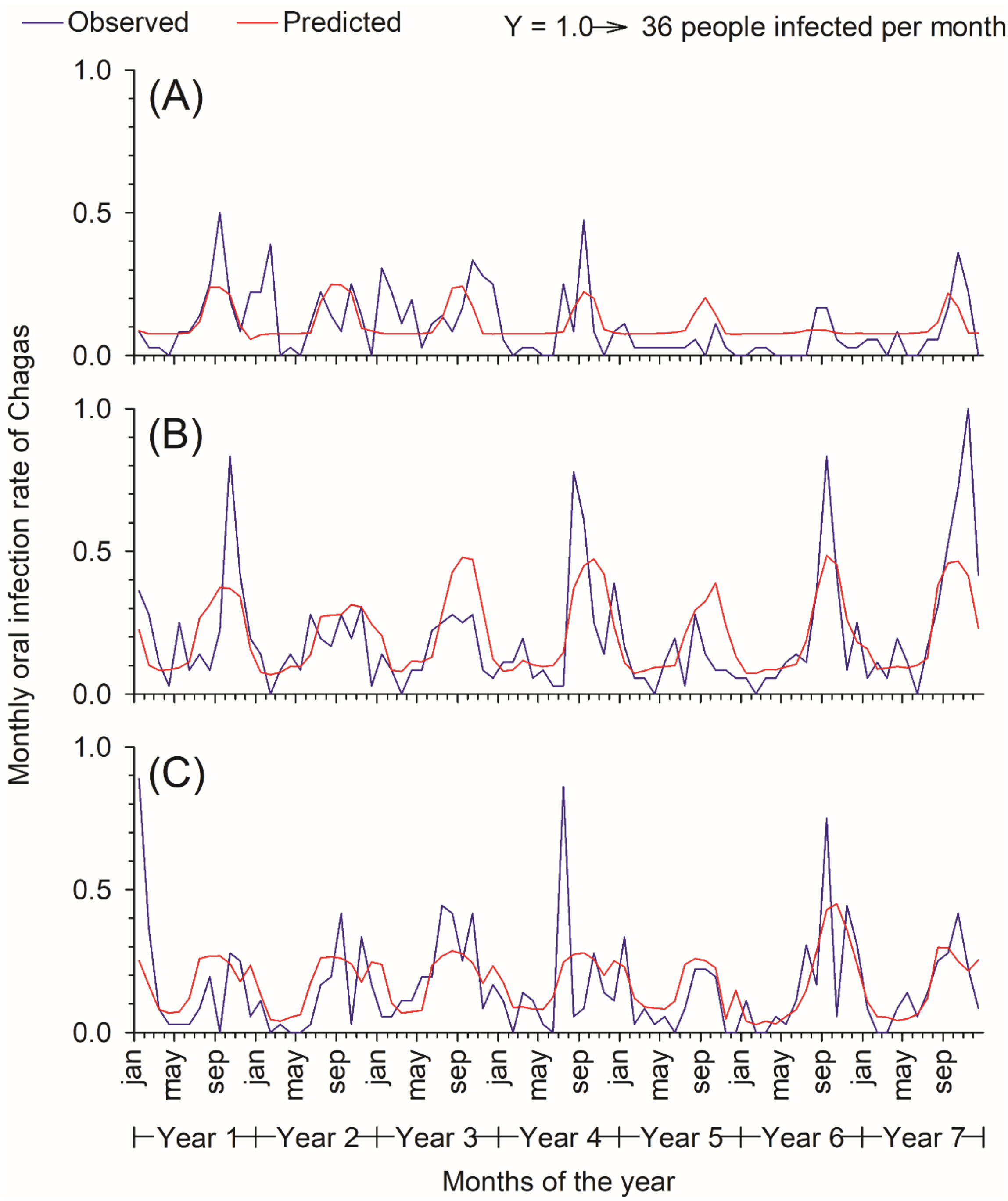

Figure 6. The Monthly oral infection rate of Chagas disease predicted by the artificial neural network (ANN) model compared to observed rates over seven years in the microregions of (A) Belém, (B) Cametá, and (C) Furos de Breves in the state of Pará, Brazil.

CHAPTER 2: Unveiling the overlooked: Current and future distribution dynamics of kissing bugs and palm species linked to oral Chagas disease transmission

ABSTRACT

Chagas disease, a neglected global health concern primarily transmitted through the bite and feces of kissing bugs, has garnered increasing attention due to recent outbreaks in northern Brazil, highlighting the role of oral transmission facilitated by the kissing bugs species *Rhodnius robustus* and *Rhodnius pictipes*. These vectors are associated with palm trees such as the maripa palm (*Attalea maripa*) and moriche palm (*Mauritia flexuosa*). In this study, we employ maximum entropy (MaxEnt) ecological niche models to analyze the spatial distribution of these vectors and palm species, predicting current and future climate suitability. Our models indicate broader potential habitats than documented occurrences, with high suitability in northern South America, southern Central America, central Africa, and southeast Asia. Projections suggest increased climate suitability by 2040, followed by a reduction by 2080. This study identifies present and future areas suitable for kissing bugs and palm tree species due to climate change, aiding in the design of prevention and management strategies.

Keywords: Neglected disease, MaxEnt, *Attalea maripa*, *Mauritia flexuosa*, *Rhodnius pictipes, Rhodnius robustus*.

1. INTRODUCTION

Chagas disease, also known as American trypanosomiasis, presents a significant global health challenge, burdening both society and economies (Guhl, 2017; Pinheiro et al., 2017; Sangenito et al., 2020). It affects 21 Latin American countries and extends its reach to areas like the US, Europe, and the Western Pacific, infecting approximately 6 to 7 million people annually and resulting in over 14,000 deaths (Bonney, 2014; World Health Organization, 2023). While primarily transmitted by the bite and feces of kissing bugs (Triatominae), Chagas disease can also spread through other means, including contaminated food consumption, blood transfusion, organ transplantation, congenital transmission, and laboratory accidents (Ferreira et al., 2018; Guhl, 2017; Sangenito et al., 2020).

Of growing concern is the emergence of oral transmission, particularly prevalent in the Amazon region due to recent outbreaks (Costa et al., 2017; Oliveira et al., 2018; Santos et al., 2020; Shikanai-Yasuda and Carvalho, 2012). These outbreaks are often linked to the ingestion of juices and products derived from palm trees, such as açaí and bacaba (Costa et al., 2017; Ferreira et al., 2018; Nóbrega et al., 2009; Oliveira et al., 2018; Ricardo-Silva et al., 2012; Santos et al., 2020). Notably, the consumption of açaí products has seen a significant annual increase in Brazil, paralleled by rising franchise sales and plantation areas (Quaresma and Euler, 2023).

The transmission of Chagas disease associated with these palm trees involves both the consumption of contaminated food and vectorial transmission by kissing bugs attracted to light sources used during fruit harvest and post-harvest activities (Costa et al., 2017; Oliveira et al., 2018; Santos et al., 2020; Shikanai-Yasuda and Carvalho, 2012). *Rhodnius robustus* Larrousse and *Rhodnius pictipes* Stål (Hemiptera: Reduviidae: Triatominae), the primary vectors of oral Chagas disease, are known to inhabit palm tree crowns and occasionally invade human homes attracted by artificial lights (Aguilar et al., 2007; Bérenger et al., 2009; Castro et al., 2010). Importantly, human dwellings do not provide suitable conditions for the survival and reproduction of *R. robustus* due to lower air humidity levels (Rocha et al., 2001).

During açaí harvesting, a surge in vector-borne infections occurs, attributed to either the production of volatile compounds mimicking female triatomine mating pheromones or the insects' attraction to light sources, leading to their accidental inclusion in açaí containers (Ferreira et al., 2018; Filigheddu et al., 2017; Guhl, 2017;

Nóbrega et al., 2009). Although kissing bugs may be present in açaí, they do not nest in these palms due to the small crown size and lack of suitable shelter and nesting sites for other animals that serve as their food sources (Dias et al., 2014; Magalhães et al., 2021).

These insects strongly associate with palm trees with large crowns, such as *Attalea maripa* (Aubl.) Mart. (maripa palm) and *Mauritia flexuosa* L. (moriche palm or buriti). In this association, they build nests that serve as habitats for reproduction and foraging, feeding on the blood of animals seeking refuge and nesting in these palm trees (Gurgel-Goncalves et al., 2012). While maripa palms are common in the Amazon rainforest and other tropical areas, moriche palms thrive in moist and swampy regions of the Amazon basin (Smith, 2015, p. 513). These palm species serve as suitable habitats for triatomines and significantly contribute to the epidemiology of Chagas disease, particularly when the distance between palms and dwellings is short (Abad-Franch et al., 2015; Abad-Franch and Gurgel-Gonçalves, 2021; Dias et al., 2014; Erazo and Cordovez, 2016; Magalhães et al., 2021).

Recognizing regions suitable for both kissing bugs and palm species involved in oral Chagas disease transmission is crucial for disease management, primarily through vector control (Shikanai-Yasuda and Carvalho, 2012). Therefore, models based on future climate change can be used in long-term planning for prevention and control measures in regions at risk of Chagas introduction, as well as warning systems, which can help prevent outbreaks by prompting public health measures (Johansson et al., 2019; Marques-Toledo et al., 2019; Rocklöv and Dubrow, 2020).

Ecological niche models (ENM), particularly based on maximum entropy (MaxEnt), are valuable tools for investigating the spatial distribution of insects and their host plants, especially in the context of global climate change (Hoberg and Brooks, 2015; Ponti and Sannolo, 2022). ENM has been used to explore the ecological aspects, distribution, and interaction of species based on its known occurrences (Calderón and González, 2020; Eberhard et al., 2020; Gurgel-Gonçalves et al., 2009; Gurgel-Gonçalves et al., 2012). Furthermore, these models allow the exploration of species evolution and potential to colonize new areas, which can be used to reduce the risk of further Chagas disease transmission (Costa et al., 2014; Garza et al., 2014; Garza et al., 2019). Despite the growing significance of oral transmission and the role of kissing bugs and palm trees, studies on their present and future geographic distribution remain scarce. Thus, this study aims to test the hypothesis that large areas worldwide, without the presence of the kissing bugs *R. robustus* and *R. pictipes*, and the palm trees *A. maripa* and *M. flexuosa*, exhibit high climatic suitability for their co-occurrence, potentially leading to oral transmission of Chagas disease.

2. MATERIAL AND METHODS

2.1. Data collection on the current geographic distribution

The species of kissing bugs studied were *Rhodnius robustus* and *R. pictipes*, which are the primary vectors of Chagas disease associated with palm trees (Guhl, 2017; Sangenito et al., 2020). The studied palm species were the maripa palm (*Attalea maripa*) and the moriche palm, or buriti (*Mauritia flexuosa*), which can host animals that serve as food sources for these insects (Browne et al., 2017; Ferreira et al., 2018; Nóbrega et al., 2009; Oliveira et al., 2018). *R. robustus* and *R. pictipes* are the main species of triatomes found in these two palm species, which makes it difficult to distinguishing between the niches occupied by each triatome (Miles et al., 1983). Therefore, the presence of by *R. pictipes* and *R. robustus* as well as maripa palm (*Attalea maripa*) and moriche palm (*Mauritia flexuosa*) serves as an biological indicator for areas that are at risk of *T. cruzi* transmission (Ricardo-Silva, 2012). Data collection for the vector insects and their palm tree hosts involved sourcing information from scientific publications, reports, and databases including the Global Biodiversity Information Facility (GBIF), Web of Science, Science Direct, Google, PubMed, and MEDLINE (Ramos et al., 2019; Santana et al., 2019). Google Earth Pro (version 7.3) was used to determine latitude and longitude when not available from the original source.

A total of 287 occurrence points were recorded for *R. robustus*, 280 for *R. pictipes*, and 3494 and 7374 for maripa and moriche palms, respectively. The data were cleansed by removing inaccurate and duplicate occurrence entries to prepare them for MaxEnt analysis. Subsequently, the Spatially Rarefy Occurrence Data tool of ArcGIS 10.8, equipped with the SDMtoolbox v. 2.5, was used to reduce spatial occurrence clusters and minimize spatial autocorrelation (Brown et al., 2017). This step was essential to optimize model predictions by avoiding overfitting to environmental biases, as models often overfit environmental biases when spatial occurrence clusters occur, lowering the model's ability to predict geographically independent data and inflating model performance values. Finally, 285 occurrence points were used for the kissing bug model, and 485 for the host palm model.

2.2. Environmental data layers for models

The WorldClim dataset version 2.1, with a spatial resolution of 2.5 arc-min (about 5 km), provided 19 bioclimatic variables for consideration (Elith et al., 2010b) (Table 1). These variables included average temperature, extreme temperatures, and rainfall data from 1970 to 2000. To address collinearity among the 19 environmental predictors, the "Explore Climate Data: Remove Highly Correlated Variables" feature of the SDMtoolbox 2.5 was utilized to identify and exclude predictors exhibiting similar patterns in explaining species habitat preference (Freeman, 2015; Santana et al., 2019). Predictors with correlation coefficients greater than 0.7 were excluded based on the methodology proposed by Elith et al. (2010b). This process allowed the selection of six uncorrelated environmental predictors for the kissing bug model and seven for the palm tree model (Table 2). The individual and joint importance of each variable in the model was determined using the Jackknife resampling method.

2.3. Future Projections

Future projections were established for two time periods, 2040 and 2080, under two alternative scenarios (SSP1-2.6 and SSP5-8.5), employing monthly average values over 20-year periods (2021-2040 and 2061-2080). Climate data were gathered from the Coupled Model Intercomparison Project Phase 6 (CMIP6), available on the WorldClim 2.1 database (Elith et al., 2010b). The SSP acronym stands for Shared Socioeconomic Pathway, representing a collection of pollutant emission scenarios affecting the climate, with low values corresponding to scenarios with lower pollutant emissions representing mild climate changes and high values presenting severer scenarios (Elith et al., 2010a). Two different scenarios were used: SSP1-2.6, considered an optimistic scenario, and SSP5-8.5, the most pessimistic one. In the optimistic scenario, carbon dioxide emissions are expected to decrease, and the temperature is expected to be 1.8°C higher by the end of the century. In contrast, emissions are expected to nearly double by 2050, with the temperature expected to be 4.4°C higher by 2100 in the most pessimistic scenario.

2.4. Model development and validation

The determination of an ecological niche model for *A. maripa* and *M. flexuosa* is due to them being among the main palm species where the *Rhodnius* kissing bug species involved in the oral transmission of Chagas disease develop (Abad-Franch and Gurgel-Gonçalves, 2021; Dias et al., 2014; Erazo and Cordovez, 2016; Magalhães et al., 2021). The determination of the ecoclimatic suitability of areas of the world is due to the fact that both insects and plants can be introduced into new regions of the world in various ways (Bonnamour et al., 2021; Fehr et al., 2020; Richardson, 2011). Furthermore, if kissing bug species are introduced to other regions of the world, they may adapt to develop in other species of palm trees that have suitable conditions (Morocoima et al., 2010; Gaunt and Miles, 2000).

The potential distribution models for the kissing bugs and the palm trees were developed using MaxEnt software (version 3.4.4) (Phillips et al., 2006). This software calculates niches and predicts global distributions by integrating presence data with environmental parameters using the maximum entropy algorithm. To improve performance, different parameter configurations and feature classes were tested using the Ecological Niche Model Evaluation (ENMeval) package in R software, version 4.2.3 (Brown et al., 2017; Muscarella et al., 2014). MaxEnt relies on two key modifiable parameters: feature classes and regularization multiplier. Feature class allows modeling of intricate relationships by mathematically transforming covariates used in the model, while regularization multiplier adds constraints to prevent over-complexity and overfitting by controlling the intensity of feature classes used. For calibration and selection of the most appropriate configuration for each model, 30 unique models with k-fold cross-validation, 10,000 background points and selected bioclimatic variables were initially created (Muscarella et al., 2014; Akaike, 1998). These models encompassed various parameter configurations, including regularization multiplier values ranging from 1 to 5 and six feature class configurations (L, LQ, H, LQH, LQHP, LQHPT), where L = linear, Q = quadratic, H = hinge, P = product, and T = threshold, as outlined in Brown et al. (2017). The best configuration was determined based on the lowest Akaike Information Criterion (AICc) score, a crucial metric for modeling species distribution (Akaike et al., 1973; Peterson et al., 2018). Model quality was assessed using the area under the curve (AUC) of the receiver operating characteristic (ROC), with values closer to 1 indicating greater predictability (Akaike, 1998;

Mandrekar, 2010). Finally, the probability (P) of locating the kissing bugs and palm trees ranges from 0 to 1 on the final model maps. This probability was categorized into three interpretive categories using the Maximum Test Sensitivity Plus Specificity Logistic Threshold (MTSPS). Probabilities of $P \geq 0.4$ were classified as highly suitable, those with $MTSPS < P < 0.4$ indicated low suitability, and $P \leq MTSPS$ were deemed unsuitable for interpretation purposes. (Liu et al., 2005; Zhang et al., 2018; Mahatara et al., 2021).

3. RESULTS

3.1. Modeling performance

The ecological niche models for *Rhodnius* kissing bugs and host palm trees exhibited AUC values of 0.966 and 0.964, respectively. The final model for the kissing bug species identified isothermality (BIO3), temperature seasonality (BIO4), minimum temperature of the coldest month (BIO6), precipitation of the warmest quarter (BIO18), precipitation of the wettest quarter (BIO16), and precipitation of the driest quarter (BIO17) as the optimal variables (Figure 1 and Table 2). Similarly, the final model for palm trees identified annual precipitation (BIO12), isothermality (BIO3), precipitation of the coldest quarter (BIO19), mean diurnal range (BIO2), annual mean temperature (BIO1), precipitation seasonality (BIO15), and precipitation of the warmest quarter (BIO18) as the optimal variables (Figure 1 and Table 2).

Isothermality (BIO3) and temperature seasonality (BIO4) were the two most influential variables in the final kissing bug model, accounting for 90% of the variance. When employed alone, BIO4 displayed the highest utility, indicating its distinct contribution to the model's performance. Similarly, annual precipitation (BIO12) and isothermality (BIO3) influenced the final palm tree model the most, accounting for 96% of the variance. BIO3 provided the most significant individual contribution to the model, as shown by a substantial decrease in gain when removed (Figure 2). The models for kissing bugs and palm trees presented areas under the curve of 0.965 and 0.963, respectively (Figure 3).

3.2. Climatic suitability change

Figure 1 illustrates the global changes in areas with suitable climates for kissing bugs and palm trees based on critical environmental variables collected from ecological niche models. For instance, locations with isothermality values up to 50 showed consistent suitability, with expansions occurring between 50 and 85. Beyond this range, suitability declined for both insects and palms (Figures 1a and 1c). Temperature seasonality values up to 400 showed reduced suitability for kissing bugs, with no additional change observed (Figure 1b). Annual precipitation values up to 900 mm demonstrated stable suitability, followed by expansions between 900 and 2900 mm and eventual decreases above this upper threshold (Figure 1d).

3.3. Current and potential distribution of kissing bugs and palm trees

Analysis of current global distributions reveals potential suitable habitats extending beyond recorded occurrences for *Rhodnius* kissing bugs and palm trees. Suitable areas for both vectors and palms are concentrated in northern South America, southern Central America, central Africa, and southeast Asia (Figure 4).

3.4. Predicted future distribution of kissing bugs and palm trees

Under both optimistic (SSP126) and pessimistic (SSP585) climate scenarios, areas in northern South America, southern Central America, central Africa, and southeast Asia are expected to have climatic suitability for both *Rhodnius* kissing bugs and palm tree species by 2040 and 2080 (Figures 5 and 6, respectively). Notably, all scenarios predict an increase in suitable regions for both species by 2040, followed by a decrease from 2040 to 2080 (Figure 7).

4. DISCUSSION

The geographic distribution of kissing bugs *Rhodnius robustus* and *Rhodnius pictipes* across 285 locations in South America, alongside the palm trees *Attalea maripa* and *Mauritia flexuosa* in 485 locations, underscores the presence of favorable conditions for these organisms. Previous studies have established that the distribution of plants and insects is influenced by both biotic and abiotic variables (Galvão and Justi, 2015; Schowalter, 2016). Notably, the distribution of these organisms predominantly aligns within the Amazon biome, characterized by a hot and humid environment with abundant rainfall and dense forest cover. The human population in these areas comprises mainly farmers, indigenous people, loggers, and extractivists, whose activities are intertwined with the forest and whose habits are linked to the oral transmission of Chagas disease (Costa et al., 2017; Oliveira et al., 2018; Shikanai-Yasuda and Carvalho, 2012).

Palm species such as maripa (*A. maripa*) and moriche palm (*M. flexuosa*) play pivotal roles in the Chagas disease transmission cycle and thrive within the diverse ecosystems found in Brazil's northern and northeastern regions. These palm trees provide shelter and nesting sites for kissing bug species, while their fruits and crowns attract animals recognized as natural reservoirs, contributing to the maintenance of the parasite's transmission cycle (Dias et al., 2014; Magalhães et al., 2021).

The area under the curve (AUC) represents the probability that the prediction made by the model is correct. Models that present AUC > 0.90, 0.80-0.90, 0.70-0.80, 0.60-0.70, and 0.50-0.60 are considered excellent, good, fair, and poor, respectively (Araujo et al., 2005; Swets, 1988). Therefore, the ecological niche models for kissing bugs and palm trees can be considered excellent, as they presented AUC values of 0.965 and 0.963, respectively. Thermal stability emerges as a crucial factor influencing the distribution of both kissing bugs and palm trees. Thermal stability is characterized by high isothermality (BIO3), indicating low variation in daytime air temperature over the year, and low temperature seasonality (BIO4), indicating minimal temperature variation, both of which are common in tropical regions and more suitable for these species (Zhang et al., 2018). Thermal variation can significantly impact various biological functions of vectors and palms, including growth, metabolism, reproduction, and the transmission ability of kissing bugs' pathogens (Margalef-Marrase et al., 2020; Rolandi and Schilman, 2012; Zhang et al., 2018).

The distribution of palm trees closely correlates with the amount of annual precipitation (BIO12), which influences soil moisture and determines water availability for existing plants (Alotaibi et al., 2023). According to model predictions, regions with moderate to high annual precipitation are most suitable for the studied palm tree species, maripa, and moriche palms. However, annual precipitation levels exceeding 3,000 mm can become detrimental to palm tree roots (Alotaibi et al., 2023).

Identifying suitable climatic conditions for kissing bugs and palm trees in northern South America, southern Central America, Central Africa, and Southeast Asia raises significant ecological and public health concerns. These areas with climatic suitability raise alarms about the potential dispersal of these insects and the risks they pose to human populations as disease vectors (Coura et al., 2002; Ricardo-Silva et al., 2012; Valente et al., 1999). While Chagas disease has traditionally been associated with Latin America, the identification of climatically suitable regions in Africa and Asia underscores the need for global surveillance of this disease and its vectors (Bonney, 2014; World Health Organization, 2023).

The movement of individuals, whether for tourism, migration, or other reasons, exposes previously naïve populations to endemic areas of Chagas disease (Portilho et al., 2020). Ecotourism, in particular, offers visitors the chance to sample native fruit juices like açaí, which may contain the protozoan parasite *T. cruzi* responsible for Chagas disease. The return of these individuals to their home regions can facilitate disease spread through various means, including blood transfusions, organ transplants, mother-to-child transmission, laboratory accidents, or infected insect bites (Ferreira et al., 2018; Pinheiro et al., 2017; Sangenito et al., 2020). Moreover, increased human presence alongside suitable habitats for palm trees heightens the likelihood of Chagas disease transmission due to greater contact with potentially infected triatomine bugs. Inadequate housing conditions, poverty, and limited healthcare access further contribute to the persistence of diseases in these areas (Bonney, 2014).

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This study also sheds light on how optimistic and pessimistic climate scenarios may impact the distribution of *Rhodnius* kissing bugs and palm species by 2040 and 2080. Significant changes are projected in regions of northern South America, southern Central America, central Africa, and Southeast Asia. These changes imply potential expansions of suitable environments for kissing bugs and palm trees, thereby altering ecological interactions, ecosystem dynamics, and potentially disease transmission.

Interestingly, the study also predicts a decrease in suitable regions for these kissing bugs and palm tree species by 2080, highlighting the dynamic nature of climate change's effects on species distribution. The size of areas with ecoclimatic suitability for *Rhodnius* kissing bugs and palm species in the period between 2040 and 2080 should be intermediate to these years.

Although MaxEnt modeling has been widely used for predicting changes in geographical distributions influenced by environmental change (Venne and Currie, 2021; Lenoir et al., 2008), some limitations can be acknowledged. A fundamental limitation is sample selection bias, since the intensity of samples varies in different areas (Phillips et al., 2009), and species may not occupy all suitable habitats (Elith et al., 2010). It is also important to note that MaxEnt only considers the influence of non-biological factors, such as climate and altitude, not other biological factors nor human activities (Cai et al., 2014; Wang et al., 2020). Despite that, MaxEnt has shown higher predictive accuracy than other methods and it performs well with either incomplete data or presence-only data (Elith et al., 2006; Phillips et al., 2006; Summers et al., 2012)

In conclusion, this study offers robust models predicting current and future global distribution areas suitable for kissing bugs and palm tree species involved in the oral transmission of Chagas disease. Temperature stability and rainfall emerge as critical variables shaping habitat suitability for kissing bugs and palm trees, warranting consideration in Chagas disease monitoring and management strategies, especially in high-risk regions.

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Table 1. Environmental variables.

Code	Description	Code	Description
BIO 1 (°C)	Annual mean temperature	BIO 11 (°C)	Mean temperature of coldest quarter
BIO 2 (°C)	Mean diurnal range (mean of monthly (max temp - min temp))	BIO 12 (mm)	Annual precipitation
BIO 3 (%)	Isothermality (BIO2/BIO7) (×100)	BIO 13 (mm)	Precipitation of wettest month
BIO 4 (°C)	Temperature seasonality (standard deviation ×100)	BIO 14 (mm)	Precipitation of driest month
BIO 5 (°C)	Max temperature of warmest month	BIO 15 (%)	Precipitation seasonality (coefficient of variation)
BIO 6 (°C)	Min temperature of coldest month	BIO 16 (mm)	Precipitation of wettest quarter
BIO 7 (°C)	Temperature annual range (bio5-bio6)	BIO 17 (mm)	Precipitation of driest quarter
BIO 8 (°C)	Mean temperature of wettest quarter	BIO 18 (mm)	Precipitation of warmest quarter
BIO 9 (°C)	Mean temperature of driest quarter	BIO 19 (mm)	Precipitation of coldest quarter
BIO 10 (°C)	Mean temperature of warmest quarter		

Table 2. Contribution (%) of the environmental variables used in the final MaxEnt models.

Environmental variable	Contribution (%)
(Kissing bug species)	
Bio 3	58.6
Bio 4	32.2
Bio 6	4.2
Bio 18	2.5
Bio 16	1.7
Bio 17	0.8

Environmental variable	Contribution (%)
(Palm tree species)	
Bio 12	58.4
Bio 3	38.1
Bio 19	1.8
Bio 2	0.9
Bio 1	0.4
Bio 15	0.3
Bio 18	0.1

Supplementary Table 1. Akaike information criterion (AIC) calculated in the ecological niche model (ENM) evaluation to select the best model setting for the kissing bugs.

Rank	FC	RM	AIC	Rank	FC	RM	AIC
1	LQ	1	7390.331	16	L	4	8091.431
2	H	1	7645.747	17	L	5	8092.574
3	LQH	1	7655.818	18	H	4	8106.331
4	LQH	2	7688.649	19	LQ	4	8109.133
5	H	2	7731.163	20	LQ	5	8138.55
6	LQ	2	7886.422	21	LQHP	5	8337.069
7	L	1	8007.708	22	LQHPT	5	8337.069
8	LQH	3	8014.632	23	LQHP	4	8412.178
9	L	2	8037.794	24	LQHPT	4	8412.178
10	H	5	8037.928	25	LQHP	3	8434.044
11	LQH	5	8047.937	26	LQHPT	3	8434.044
12	LQ	3	8068.773	27	LQHP	2	8713.12
13	LQH	4	8072.745	28	LQHPT	2	8715.625
14	H	3	8073.956	29	LQHPT	1	9833.245
15	L	3	8076.703	30	LQHP	1	10086.73

In the header: FC = feature classes where (L= linear, Q= quadratic, H= hinge, P= product, and T= threshold) e RM = regularization multiplier.

Supplementary Table 2. Akaike information criterion calculated in the ENM eval to select the best model setting for the palm trees.

Rank	FC	RM	AIC	Rank	FC	RM	AIC
1	LQH	1	13466.09	16	LQ	1	14194.52
2	H	1	13498.53	17	LQHP	4	14218.98
3	LQHP	1	13609.56	18	LQH	5	14237.97
4	LQHPT	1	13759.08	19	L	1	14258.91
5	LQH	2	13853.71	20	LQHPT	4	14271.67
6	H	2	13857.42	21	L	2	14280.92
7	LQHP	2	13876.54	22	LQHP	5	14300.07
8	H	3	13892.88	23	L	3	14304.86
9	H	5	13910.79	24	L	4	14329.69
10	H	4	13962.94	25	LQHPT	5	14344.95
11	LQHPT	2	13974.3	26	L	5	14354.64
12	LQH	3	14043.68	27	LQ	2	14425.66
13	LQHP	3	14079.23	28	LQ	3	14437.84
14	LQH	4	14173.15	29	LQ	4	14449.89
15	LQHPT	3	14178.52	30	LQ	5	14461.92

In the header: FC = feature classes where (L= linear, Q= quadratic, H= hinge, P= product, and T= threshold) e RM = regularization multiplier.

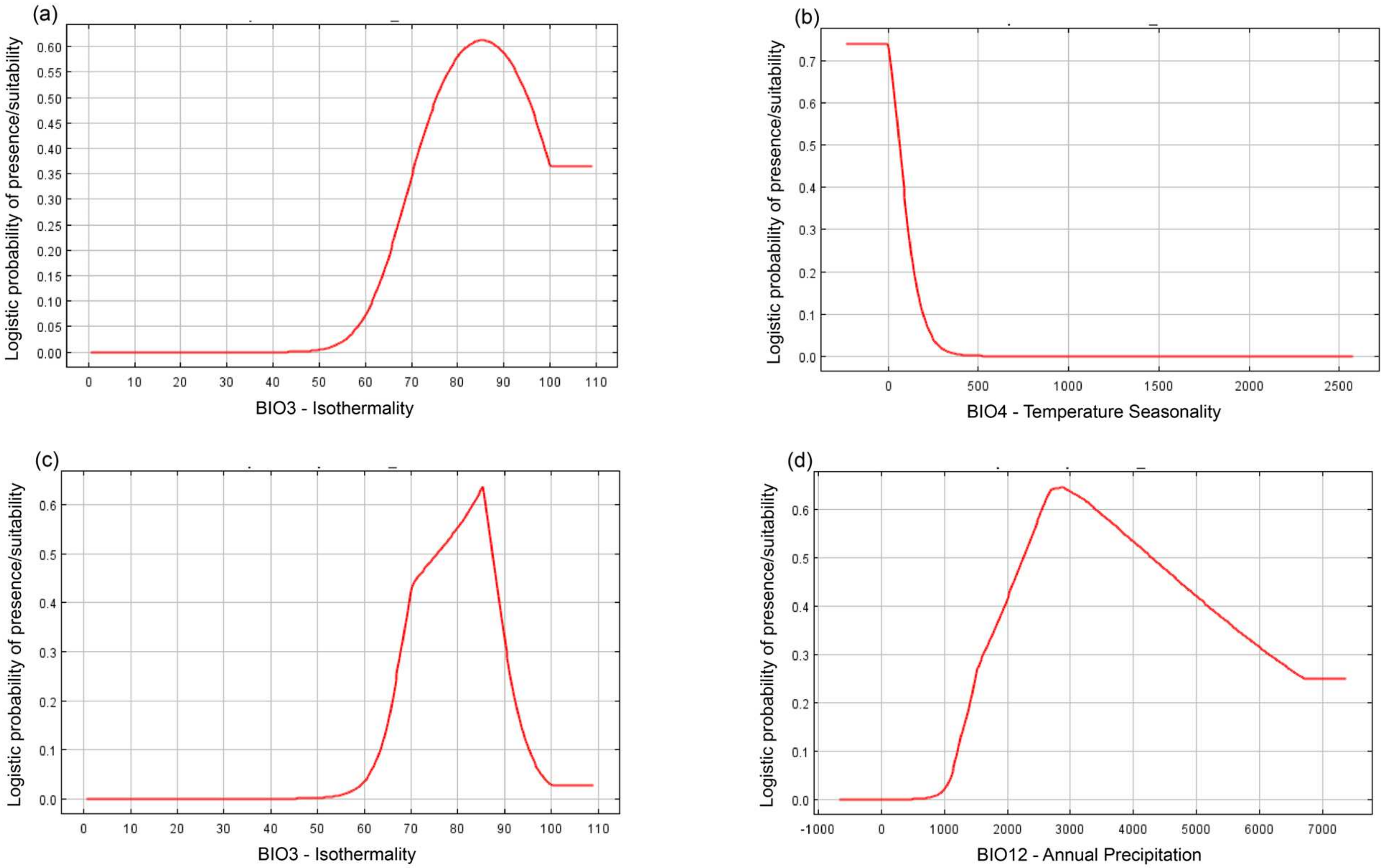


Figure 1. Temporal variation in the climatically suitable areas for *Rhodnius* kissing bug species based on (a) isothermality and (b) temperature seasonality, and for palm trees species based on (c) isothermality and (d) annual precipitation on a global scale.

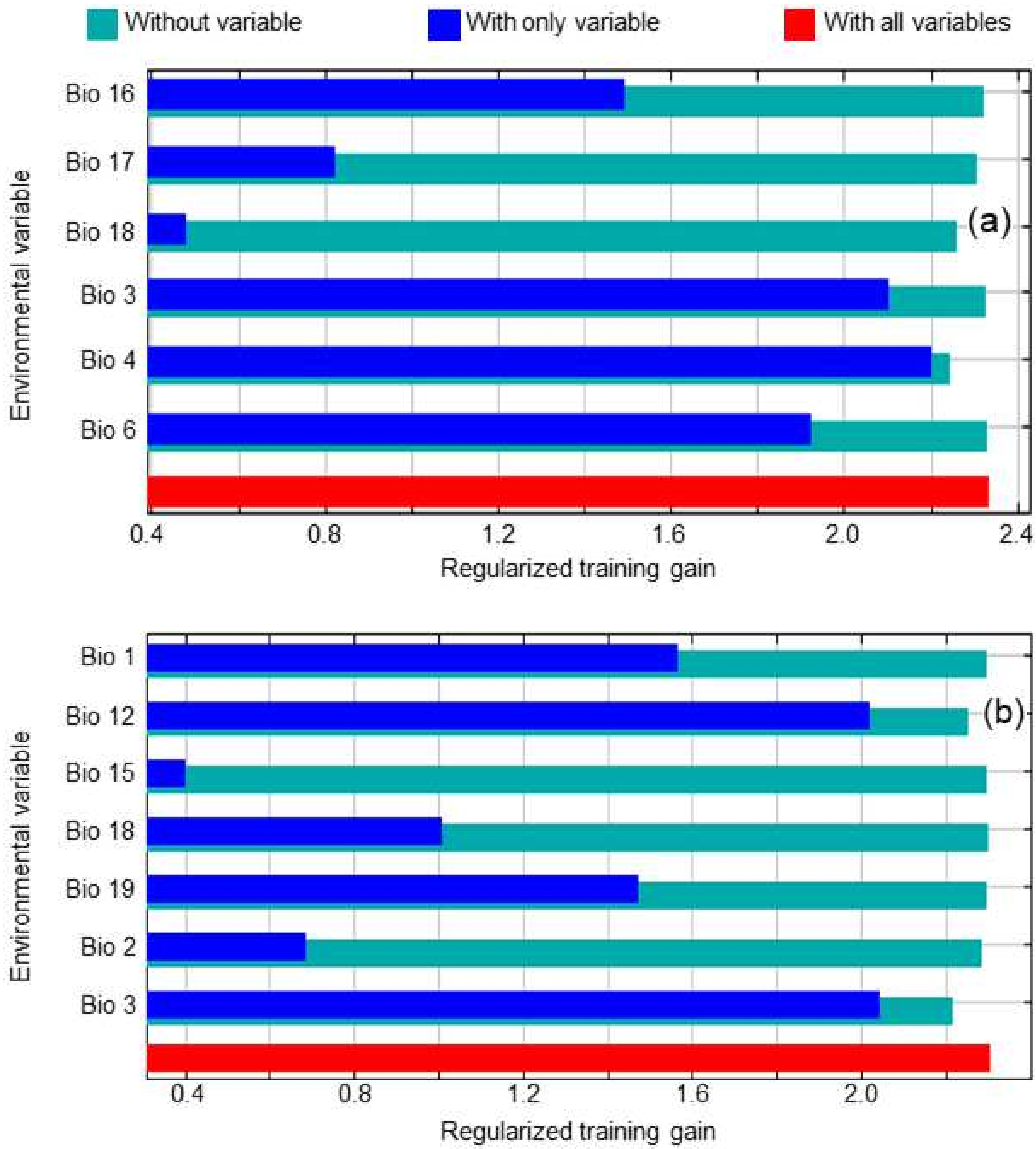


Figure 2. Relative importance of environmental variables in the final ecological niche models for (a) *Rhodnius* kissing bug (b) palm trees species using the Jackknife resampling method.

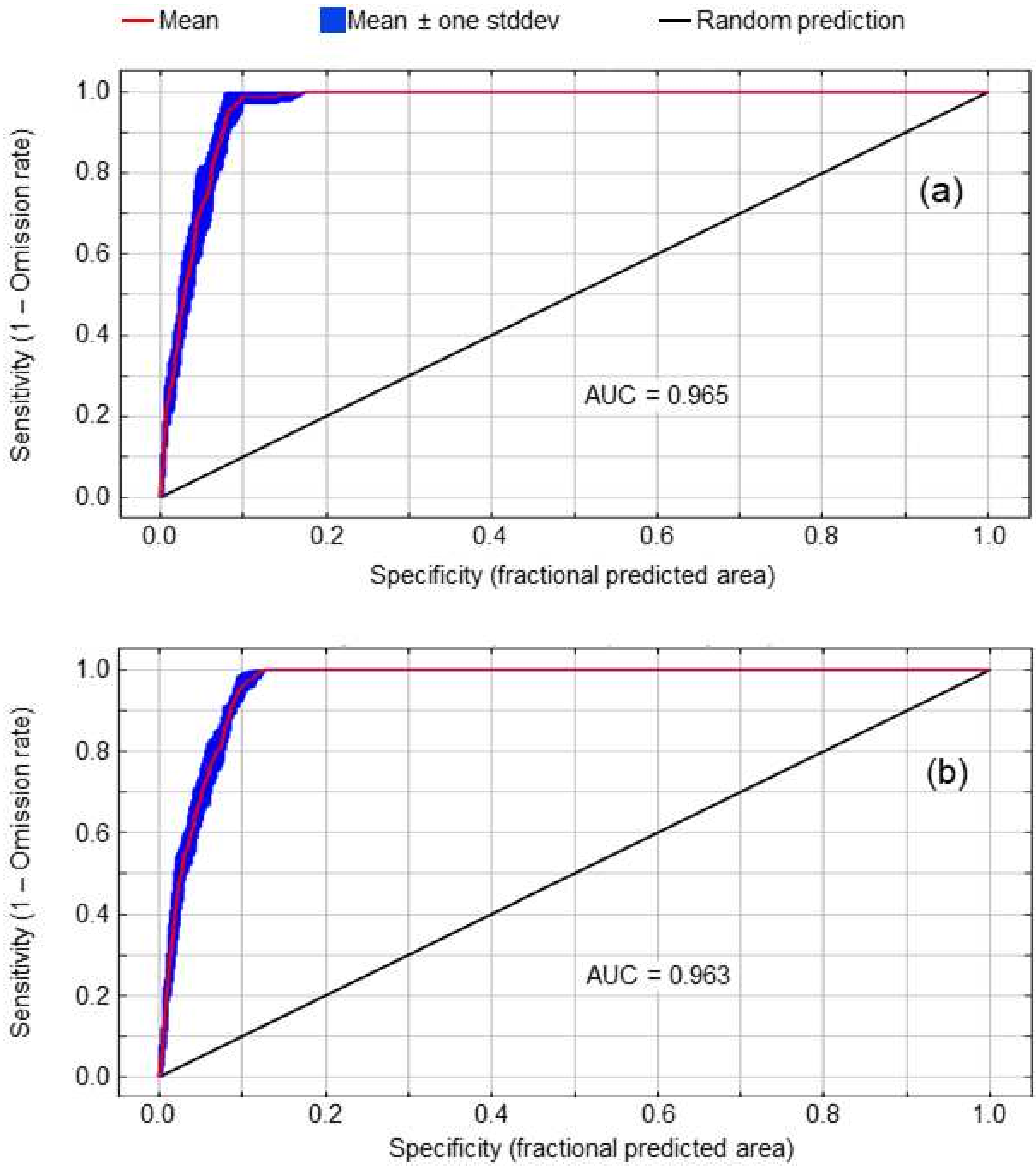


Figure 3. Repeated operating characteristic curve of ecological niche models for (a) *Rhodnius* kissing bug (b) palm trees species.

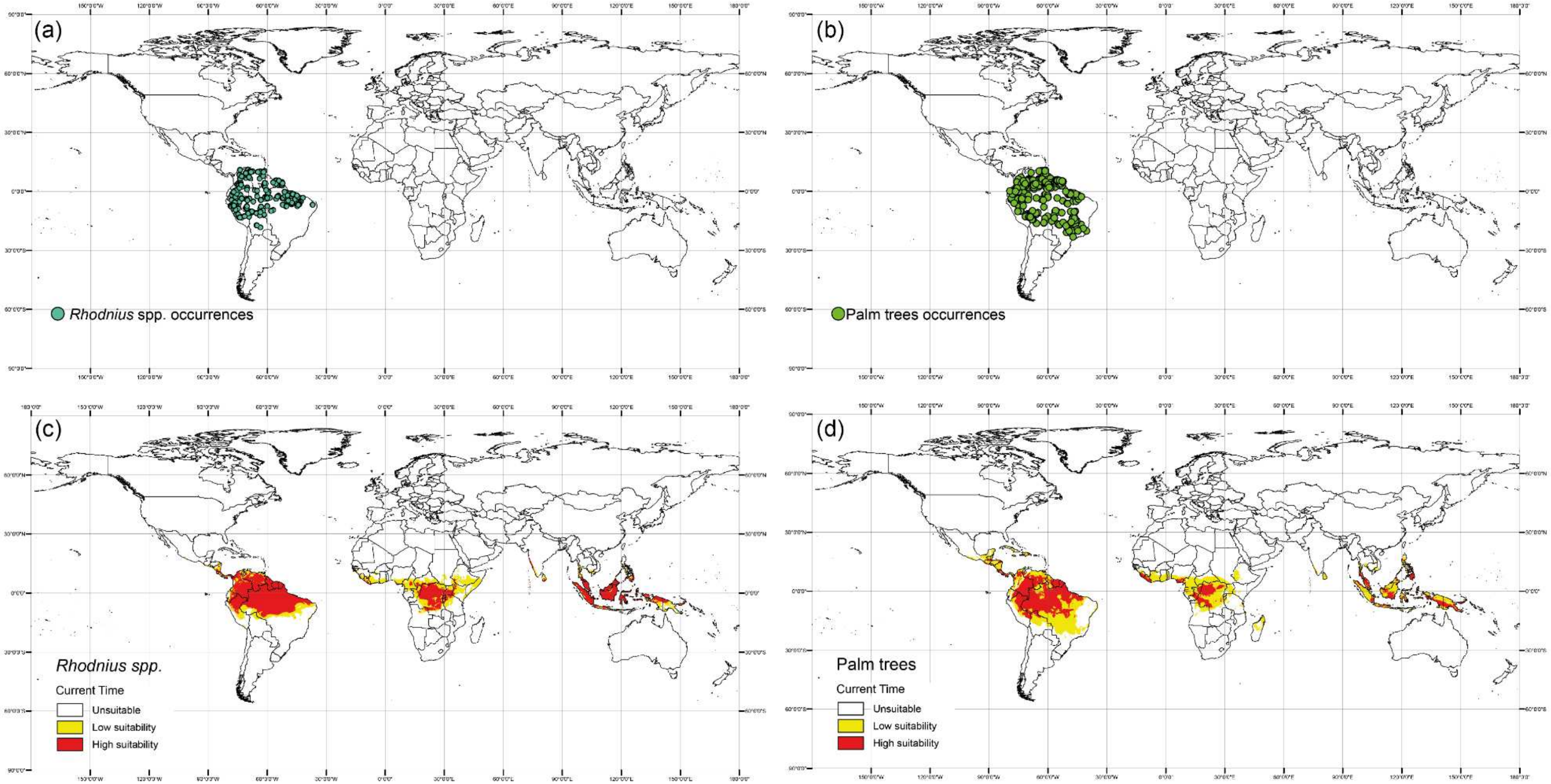


Figure 4. Current geographical distribution of the kissing bug species *Rhodnius robustus* and *Rhodnius pictipes (a)*, geographical distribution of the palm tree species, maripa (*Attalea maripa*) and moriche (*Mauritia flexuosa*) (b), and potentially suitable areas for them at present (c and d). In white, unsuitable areas; in yellow, areas with low suitability; and in red, areas with high sui tability.

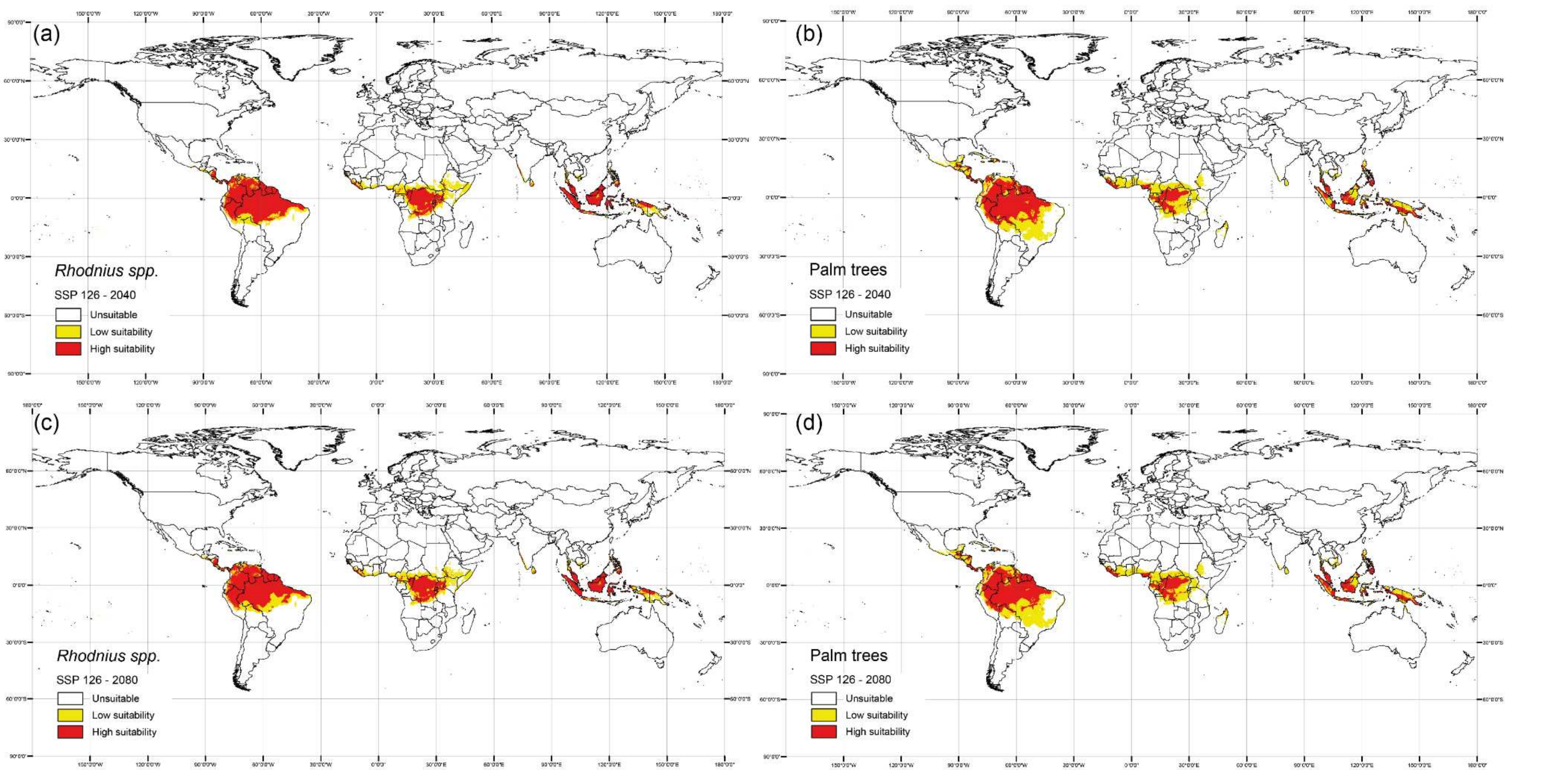


Figure 5. Future projections for 2040 and 2080 for the kissing bug species *Rhodnius robustus* and *Rhodnius pictipes* (a, c), and the palm tree species, maripa (*Attalea maripa*) and moriche (*Mauritia flexuosa*) (b, d) using the MaxEnt model running on the MIROC6 (GCM) considering the most optimistic scenario (SSP126). In white, unsuitable areas; in yellow, areas with low suitability; and in red, areas with high suitability.

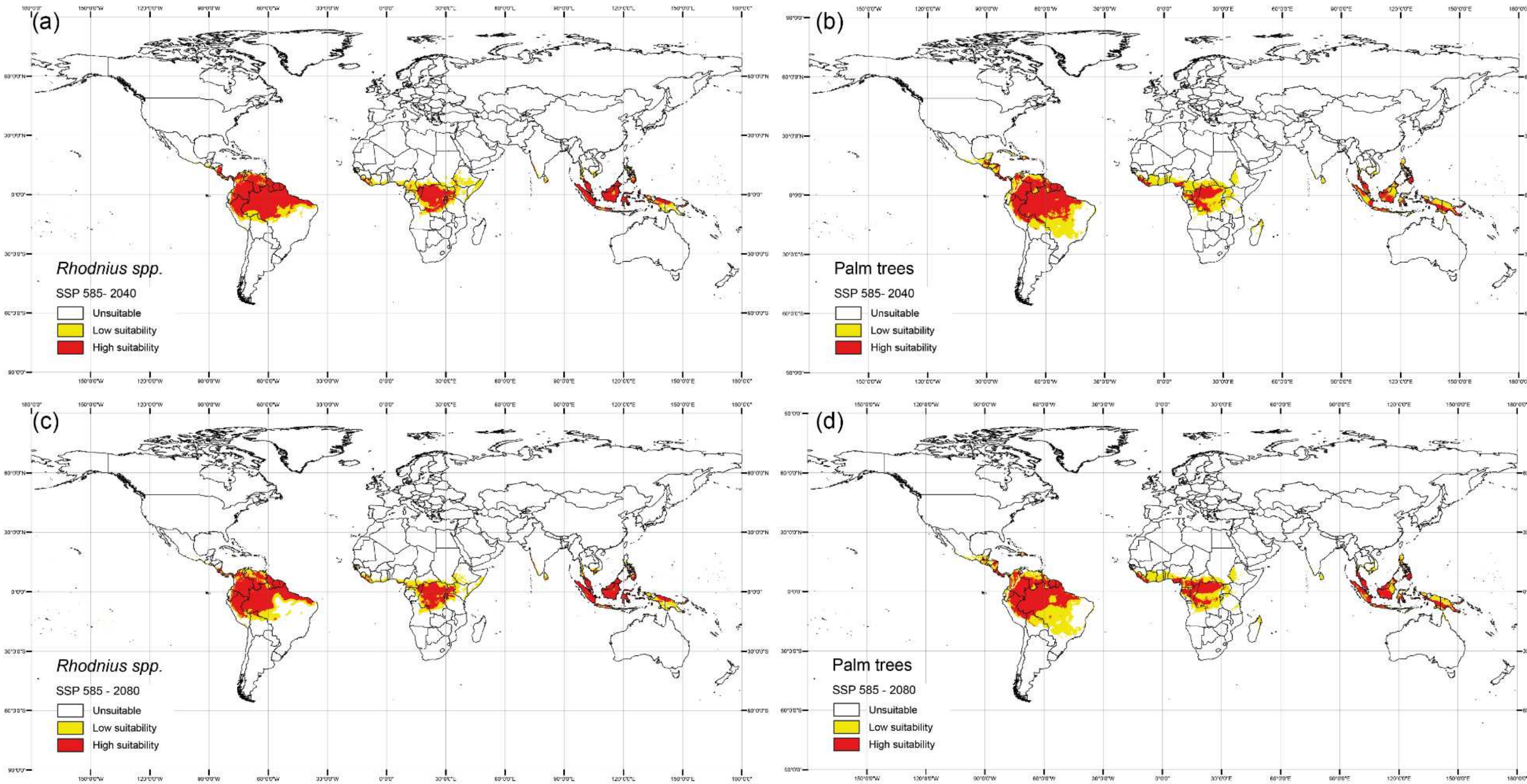
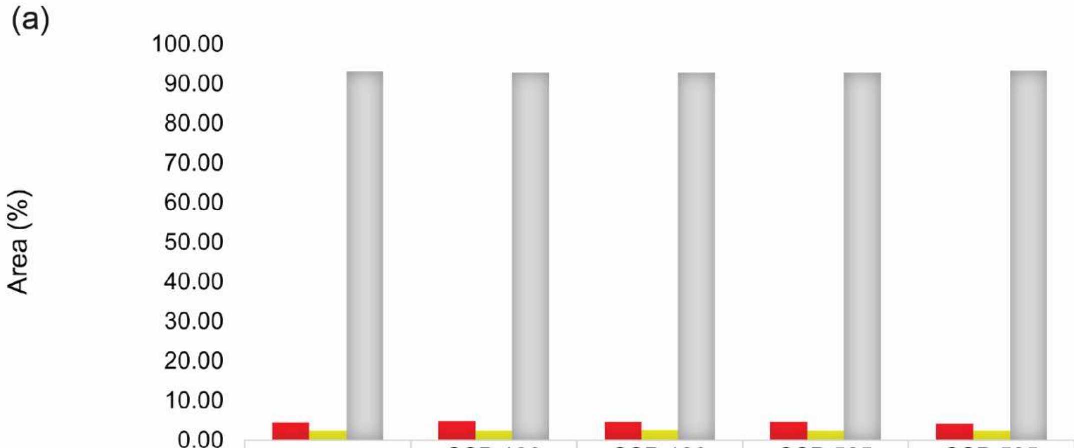
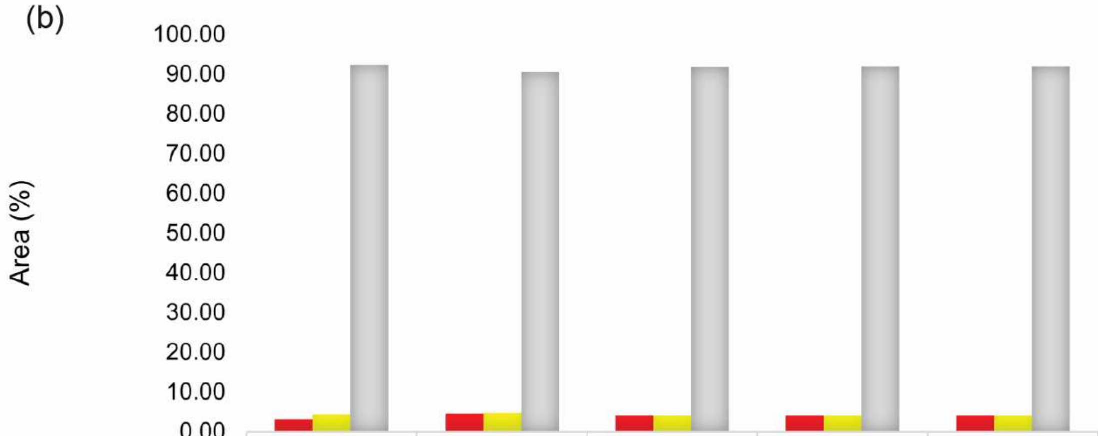


Figure 6. Future projections for 2040 and 2080 for the kissing bug species *Rhodnius robustus* and *Rhodnius pictipes* (a, c), and the palm tree species, maripa (*Attalea maripa*) and moriche (*Mauritia flexuosa*) using the MaxEnt model running MIROC6 (GCM) considering the most pessimistic scenario (SSP585). In white, unsuitable areas; in yellow, areas with low suitability; and in red, areas with high suitability.



	CT	SSP 126 2040	SSP 126 2080	SSP 585 2040	SSP 585 2080
High suitability (%)	4.42	4.74	4.63	4.66	4.20
Low suitability (%)	2.40	2.42	2.53	2.47	2.42
Unsuitable (%)	93.18	92.84	92.83	92.87	93.38



	CT	SSP 126 2040	SSP 126 2080	SSP 585 2040	SSP 585 2080
High suitability (%)	3.21	4.58	4.01	4.05	3.99
Low suitability (%)	4.36	4.74	4.08	4.00	4.02
Unsuitable (%)	92.43	90.68	91.91	91.96	91.98

Figure 7. Area percentage suitability for the kissing bug species *Rhodnius robustus* and *Rhodnius pictipes* (a), and for the palm tree species *Attalea maripa* (i.e., maripa) and *Mauritia flexuosa* (i.e., moriche) (b). *CT= Current time, SSP126 2040= optimistic scenario for 2040, SSP126 2080= optimistic scenario for 2080, SSP585 2040= pessimistic scenario for 2040, SSP585 2080= pessimistic scenario for 2080.

GENERAL CONCLUSIONS

The artificial neural network model developed in this study is effective for predicting the oral transmission rate of Chagas disease. It accurately predicts transmission rates across different regions and periods, with key influencing factors including the size of açaí plantation areas, time after the start of the açaí harvest, air temperature, rainfall, wind speed, and atmospheric pressure.

In addition, robust ecological niche models were determined that predict current and future global distribution areas suitable for kissing bugs and palm species involved in the oral transmission of Chagas disease. Temperature stability and rainfall are important variables that shape the habitat suitability of kissing bugs and palm trees and must be taken into consideration for Chagas disease monitoring and management strategies, especially in high-risk regions.